Santodonato, L., et al., Gene Therapy 4:1246-1255 (1997); and Zhang, J.-F. et al., Cancer Gene Therapy 3: 31-38 (1996)), which are herein incorporated by reference. In one embodiment, the cells which are engineered are arterial cells. The arterial cells may be reintroduced into the patient through direct injection to the artery, the tissues surrounding the artery, or through catheter injection.

As discussed in more detail below, the polynucleotide constructs can be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, and the like). The polynucleotide constructs may be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

In one embodiment, the polynucleotide of the present invention is delivered as a naked polynucleotide. The term "naked" polynucleotide, DNA or RNA refers to sequences that are free from any delivery vehicle that acts to assist, promote or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotide of the present invention can also be delivered in liposome formulations and lipofectin formulations and the like can be prepared by methods well known to those skilled in the art. Such methods are described, for example, in U.S. Patent Nos. 5,593,972, 5,589,466, and 5,580,859, which are herein incorporated by reference.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Appropriate vectors include pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; pSVK3, pBPV, pMSG and pSVL available from Pharmacia; and pEF1/V5, pcDNA3.1, and pRc/CMV2 available from Invitrogen. Other suitable vectors will be readily apparent to the skilled artisan.

Any strong promoter known to those skilled in the art can be used for driving the expression of the polynucleotide sequence. Suitable promoters include adenoviral promoters, such as the adenoviral major late promoter; or heterologous promoters, such as the cytomegalovirus (CMV) promoter; the respiratory syncytial virus (RSV) promoter; inducible promoters, such as the MMT promoter, the metallothionein promoter; heat shock promoters; the albumin promoter; the ApoAI promoter; human globin promoters; viral thymidine kinase promoters, such as the Herpes Simplex thymidine kinase promoter; retroviral LTRs; the b-

actin promoter; and human growth hormone promoters. The promoter also may be the native promoter for the polynucleotide of the present invention.

Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular, fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked nucleic acid sequence injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 mg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration.

The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues,

throat or mucous membranes of the nose. In addition, naked DNA constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The naked polynucleotides are delivered by any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, and so-called "gene guns". These delivery methods are known in the art.

The constructs may also be delivered with delivery vehicles such as viral sequences, viral particles, liposome formulations, lipofectin, precipitating agents, etc. Such methods of delivery are known in the art.

In certain embodiments, the polynucleotide constructs are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations. However, cationic liposomes are particularly preferred because a tight charge complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA (1989) 86:6077-6081, which is herein incorporated by reference); and purified transcription factors (Debs et al., J. Biol. Chem. (1990) 265:10189-10192, which is herein incorporated by reference), in functional form.

Cationic liposomes are readily available. For example, N[1-2,3-dioleyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are particularly useful and are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, N.Y. (See, also, Felgner et al., Proc. Natl Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference). Other commercially available liposomes include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication No. WO 90/11092 (which is herein incorporated by reference) for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes is explained in the literature, see, e.g., P. Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417, which is herein incorporated by reference. Similar methods can be used to prepare liposomes from other cationic lipid materials.

Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl, choline, cholesterol, phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), dioleoylphoshatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP starting materials in appropriate ratios. Methods for making liposomes using these materials are well known in the art.

For example, commercially dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can be used in various combinations to make conventional liposomes, with or without the addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome-nucleic acid complexes are prepared using methods well known in the art. See, e.g., Straubinger et al., Methods of Immunology (1983), 101:512-527, which is herein incorporated by reference. For example, MLVs containing nucleic acid can be prepared by depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to

the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include Ca^{2+}-EDTA chelation (Papahadjopoulos et al., Biochim. Biophys. Acta (1975) 394:483; Wilson et al., Cell (1979) 17:77); ether injection (Deamer, D. and Bangham, A., Biochim. Biophys. Acta (1976) 443:629; Ostro et al., Biochem. Biophys. Res. Commun. (1977) 76:836; Fraley et al., Proc. Natl. Acad. Sci. USA (1979) 76:3348); detergent dialysis (Enoch, H. and Strittmatter, P., Proc. Natl. Acad. Sci. USA (1979) 76:145); and reverse-phase evaporation (REV) (Fraley et al., J. Biol. Chem. (1980) 255:10431; Szoka, F. and Papahadjopoulos, D., Proc. Natl. Acad. Sci. USA (1978) 75:145; Schaefer-Ridder et al., Science (1982) 215:166), which are herein incorporated by reference.

Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ration will be from about 5:1 to about 1:5. More preferably, the ration will be about 3:1 to about 1:3. Still more preferably, the ratio will be about 1:1.

U.S. Patent No. 5,676,954 (which is herein incorporated by reference) reports on the injection of genetic material, complexed with cationic liposomes carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide methods for delivering DNA-cationic lipid complexes to mammals.

In certain embodiments, cells are engineered, ex vivo or in vivo, using a retroviral particle containing RNA which comprises a sequence encoding a polypeptide of the present invention. Retroviruses from which the retroviral plasmid vectors may be derived include, but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, Rous sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the PE501, PA317, R-2, R-AM, PA12, T19-14X, VT-19-17-H2, RCRE, RCRIP, GP+E-86, GP+envAm12, and DAN cell lines as described in Miller, Human Gene Therapy 1:5-14 (1990), which is incorporated herein by reference in its entirety. The vector

may transduce the packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and $CaPO_4$ precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

The producer cell line generates infectious retroviral vector particles which include polynucleotide encoding a polypeptide of the present invention. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either in vitro or in vivo. The transduced eukaryotic cells will express a polypeptide of the present invention.

In certain other embodiments, cells are engineered, ex vivo or in vivo, with polynucleotide contained in an adenovirus vector. Adenovirus can be manipulated such that it encodes and expresses a polypeptide of the present invention, and at the same time is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. Adenovirus expression is achieved without integration of the viral DNA into the host cell chromosome, thereby alleviating concerns about insertional mutagenesis. Furthermore, adenoviruses have been used as live enteric vaccines for many years with an excellent safety profile (Schwartz, A. R. et al. (1974) Am. Rev. Respir. Dis.109:233-238). Finally, adenovirus mediated gene transfer has been demonstrated in a number of instances including transfer of alpha-1-antitrypsin and CFTR to the lungs of cotton rats (Rosenfeld, M. A. et al. (1991) Science 252:431-434; Rosenfeld et al., (1992) Cell 68:143-155). Furthermore, extensive studies to attempt to establish adenovirus as a causative agent in human cancer were uniformly negative (Green, M. et al. (1979) Proc. Natl. Acad. Sci. USA 76:6606).

Suitable adenoviral vectors useful in the present invention are described, for example, in Kozarsky and Wilson, Curr. Opin. Genet. Devel. 3:499-503 (1993); Rosenfeld et al., Cell 68:143-155 (1992); Engelhardt et al., Human Genet. Ther. 4:759-769 (1993); Yang et al., Nature Genet. 7:362-369 (1994); Wilson et al., Nature 365:691-692 (1993); and U.S. Patent No. 5,652,224, which are herein incorporated by reference. For example, the adenovirus vector Ad2 is useful and can be grown in human 293 cells. These cells contain the E1 region of adenovirus and constitutively express Ela and Elb, which complement the defective adenoviruses by providing the products of the genes deleted from the vector. In addition to Ad2, other varieties of adenovirus (e.g., Ad3, Ad5, and Ad7) are also useful in the present invention.

Preferably, the adenoviruses used in the present invention are replication deficient. Replication deficient adenoviruses require the aid of a helper virus and/or packaging cell line to form infectious particles. The resulting virus is capable of infecting cells and can express a polynucleotide of interest which is operably linked to a promoter, but cannot replicate in most cells. Replication deficient adenoviruses may be deleted in one or more of all or a portion of the following genes: E1a, E1b, E3, E4, E2a, or L1 through L5.

In certain other embodiments, the cells are engineered, ex vivo or in vivo, using an adeno-associated virus (AAV). AAVs are naturally occurring defective viruses that require helper viruses to produce infectious particles (Muzyczka, N., Curr. Topics in Microbiol. Immunol. 158:97 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells. Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate, but space for exogenous DNA is limited to about 4.5 kb. Methods for producing and using such AAVs are known in the art. See, for example, U.S. Patent Nos. 5,139,941, 5,173,414, 5,354,678, 5,436,146, 5,474,935, 5,478,745, and 5,589,377.

For example, an appropriate AAV vector for use in the present invention will include all the sequences necessary for DNA replication, encapsidation, and host-cell integration. The polynucleotide construct is inserted into the AAV vector using standard cloning methods, such as those found in Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (1989). The recombinant AAV vector is then transfected into packaging cells which are infected with a helper virus, using any standard technique, including lipofection, electroporation, calcium phosphate precipitation, etc. Appropriate helper viruses include adenoviruses, cytomegaloviruses, vaccinia viruses, or herpes viruses. Once the packaging cells are transfected and infected, they will produce infectious AAV viral particles which contain the polynucleotide construct. These viral particles are then used to transduce eukaryotic cells, either ex vivo or in vivo. The transduced cells will contain the polynucleotide construct integrated into its genome, and will express a polypeptide of the invention.

Another method of gene therapy involves operably associating heterologous control regions and endogenous polynucleotide sequences (e.g. encoding a polypeptide of the present invention) via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc.

Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not normally expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made, using standard techniques known in the art, which contain the promoter with targeting sequences flanking the promoter. Suitable promoters are described herein. The targeting sequence is sufficiently complementary to an endogenous sequence to permit homologous recombination of the promoter-targeting sequence with the endogenous sequence. The targeting sequence will be sufficiently near the 5' end of the desired endogenous polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination.

The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter. The amplified promoter and targeting sequences are digested and ligated together.

The promoter-targeting sequence construct is delivered to the cells, either as naked polynucleotide, or in conjunction with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, whole viruses, lipofection, precipitating agents, etc., described in more detail above. The P promoter-targeting sequence can be delivered by any method, included direct needle injection, intravenous injection, topical administration, catheter infusion, particle accelerators, etc. The methods are described in more detail below.

The promoter-targeting sequence construct is taken up by cells. Homologous recombination between the construct and the endogenous sequence takes place, such that an endogenous sequence is placed under the control of the promoter. The promoter then drives the expression of the endogenous sequence.

Preferably, the polynucleotide encoding a polypeptide of the present invention contains a secretory signal sequence that facilitates secretion of the protein. Typically, the signal sequence is positioned in the coding region of the polynucleotide to be expressed towards or at the 5' end of the coding region. The signal sequence may be homologous or heterologous to the polynucleotide of interest and may be homologous or heterologous to the

cells to be transfected. Additionally, the signal sequence may be chemically synthesized using methods known in the art.

Any mode of administration of any of the above-described polynucleotides constructs can be used so long as the mode results in the expression of one or more molecules in an amount sufficient to provide a therapeutic effect. This includes direct needle injection, systemic injection, catheter infusion, biolistic injectors, particle accelerators (i.e., "gene guns"), gelfoam sponge depots, other commercially available depot materials, osmotic pumps (e.g., Alza minipumps), oral or suppositorial solid (tablet or pill) pharmaceutical formulations, and decanting or topical applications during surgery. For example, direct injection of naked calcium phosphate-precipitated plasmid into rat liver and rat spleen or a protein-coated plasmid into the portal vein has resulted in gene expression of the foreign gene in the rat livers (Kaneda et al., Science 243:375 (1989)).

A preferred method of local administration is by direct injection. Preferably, a recombinant molecule of the present invention complexed with a delivery vehicle is administered by direct injection into or locally within the area of arteries. Administration of a composition locally within the area of arteries refers to injecting the composition centimeters and preferably, millimeters within arteries.

Another method of local administration is to contact a polynucleotide construct of the present invention in or around a surgical wound. For example, a patient can undergo surgery and the polynucleotide construct can be coated on the surface of tissue inside the wound or the construct can be injected into areas of tissue inside the wound.

Therapeutic compositions useful in systemic administration, include recombinant molecules of the present invention complexed to a targeted delivery vehicle of the present invention. Suitable delivery vehicles for use with systemic administration comprise liposomes comprising ligands for targeting the vehicle to a particular site.

Preferred methods of systemic administration, include intravenous injection, aerosol, oral and percutaneous (topical) delivery. Intravenous injections can be performed using methods standard in the art. Aerosol delivery can also be performed using methods standard in the art (see, for example, Stribling et al., Proc. Natl. Acad. Sci. USA 189:11277-11281, 1992, which is incorporated herein by reference). Oral delivery can be performed by complexing a polynucleotide construct of the present invention to a carrier capable of withstanding degradation by digestive enzymes in the gut of an animal. Examples of such

carriers, include plastic capsules or tablets, such as those known in the art. Topical delivery can be performed by mixing a polynucleotide construct of the present invention with a lipophilic reagent (e.g., DMSO) that is capable of passing into the skin.

Determining an effective amount of substance to be delivered can depend upon a number of factors including, for example, the chemical structure and biological activity of the substance, the age and weight of the animal, the precise condition requiring treatment and its severity, and the route of administration. The frequency of treatments depends upon a number of factors, such as the amount of polynucleotide constructs administered per dose, as well as the health and history of the subject. The precise amount, number of doses, and timing of doses will be determined by the attending physician or veterinarian.

Therapeutic compositions of the present invention can be administered to any animal, preferably to mammals and birds. Preferred mammals include humans, dogs, cats, mice, rats, rabbits sheep, cattle, horses and pigs, with humans being particularly preferred.

Biological Activities

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, can be used in assays to test for one or more biological activities. If these polynucleotides or polypeptides, or agonists or antagonists of the present invention, do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides, and agonists or antagonists could be used to treat the associated disease.

Immune Activity

A polypeptide or polynucleotide, or agonists or antagonists of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, polynucleotides or polypeptides, or

agonists or antagonists of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. Polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

Moreover, polynucleotides or polypeptides, or agonists or antagonists of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, polynucleotides or polypeptides, or agonists or antagonists of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of polynucleotides or polypeptides, or agonists or antagonists of the present invention that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitis, and autoimmune inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The administration of polynucleotides or polypeptides, or agonists or antagonists of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to modulate inflammation. For example, polynucleotides or polypeptides, or agonists or antagonists of the present invention may inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including chronic prostatitis, granulomatous prostatitis and malacoplakia, inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

Hyperproliferative Disorders

Polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used to treat or detect hyperproliferative disorders, including neoplasms. Polynucleotides or polypeptides, or agonists or antagonists of the present invention may inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, Polynucleotides or polypeptides, or agonists or antagonists of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by Polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to neoplasms located in the: colon, abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstron's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

One preferred embodiment utilizes polynucleotides of the present invention to inhibit aberrant cellular division, by gene therapy using the present invention, and/or protein fusions or fragments thereof.

Thus, the present invention provides a method for treating cell proliferative disorders by inserting into an abnormally proliferating cell a polynucleotide of the present invention, wherein said polynucleotide represses said expression.

Another embodiment of the present invention provides a method of treating cell-proliferative disorders in individuals comprising administration of one or more active gene copies of the present invention to an abnormally proliferating cell or cells. In a preferred embodiment, polynucleotides of the present invention is a DNA construct comprising a recombinant expression vector effective in expressing a DNA sequence encoding said polynucleotides. In another preferred embodiment of the present invention, the DNA construct encoding the poynucleotides of the present invention is inserted into cells to be treated utilizing a retrovirus, or more preferrably an adenoviral vector (See G J. Nabel, et. al., PNAS 1999 96: 324-326, which is hereby incorporated by reference). In a most preferred embodiment, the viral vector is defective and will not transform non-proliferating cells, only proliferating cells. Moreover, in a preferred embodiment, the polynucleotides of the present invention inserted into proliferating cells either alone, or in combination with or fused to other polynucleotides, can then be modulated via an external stimulus (i.e. magnetic, specific small molecule, chemical, or drug administration, etc.), which acts upon the promoter upstream of said polynucleotides to induce expression of the encoded protein product. As such the beneficial therapeutic affect of the present invention may be expressly modulated (i.e. to increase, decrease, or inhibit expression of the present invention) based upon said external stimulus.

Polynucleotides of the present invention may be useful in repressing expression of oncogenic genes or antigens. By "repressing expression of the oncogenic genes " is intended the suppression of the transcription of the gene, the degradation of the gene transcript (pre-message RNA), the inhibition of splicing, the destruction of the messenger RNA, the prevention of the post-translational modifications of the protein, the destruction of the protein, or the inhibition of the normal function of the protein.

For local administration to abnormally proliferating cells, polynucleotides of the present invention may be administered by any method known to those of skill in the art including, but not limited to transfection, electroporation, microinjection of cells, or in vehicles such as liposomes, lipofectin, or as naked polynucleotides, or any other method described throughout the specification. The polynucleotide of the present invention may be delivered by known gene delivery systems such as, but not limited to, retroviral vectors (Gilboa, J. Virology 44:845 (1982); Hocke, Nature 320:275 (1986); Wilson, et al., Proc. Natl. Acad. Sci. U.S.A. 85:3014), vaccinia virus system (Chakrabarty et al., Mol. Cell Biol. 5:3403

(1985) or other efficient DNA delivery systems (Yates et al., Nature 313:812 (1985)) known to those skilled in the art. These references are exemplary only and are hereby incorporated by reference. In order to specifically deliver or transfect cells which are abnormally proliferating and spare non-dividing cells, it is preferable to utilize a retrovirus, or adenoviral (as described in the art and elsewhere herein) delivery system known to those of skill in the art. Since host DNA replication is required for retroviral DNA to integrate and the retrovirus will be unable to self replicate due to the lack of the retrovirus genes needed for its life cycle. Utilizing such a retroviral delivery system for polynucleotides of the present invention will target said gene and constructs to abnormally proliferating cells and will spare the non-dividing normal cells.

The polynucleotides of the present invention may be delivered directly to cell proliferative disorder/disease sites in internal organs, body cavities and the like by use of imaging devices used to guide an injecting needle directly to the disease site. The polynucleotides of the present invention may also be administered to disease sites at the time of surgical intervention.

By "cell proliferative disease" is meant any human or animal disease or disorder, affecting any one or any combination of organs, cavities, or body parts, which is characterized by single or multiple local abnormal proliferations of cells, groups of cells, or tissues, whether benign or malignant.

Any amount of the polynucleotides of the present invention may be administered as long as it has a biologically inhibiting effect on the proliferation of the treated cells. Moreover, it is possible to administer more than one of the polynucleotide of the present invention simultaneously to the same site. By "biologically inhibiting" is meant partial or total growth inhibition as well as decreases in the rate of proliferation or growth of the cells. The biologically inhibitory dose may be determined by assessing the effects of the polynucleotides of the present invention on target malignant or abnormally proliferating cell growth in tissue culture, tumor growth in animals and cell cultures, or any other method known to one of ordinary skill in the art.

The present invention is further directed to antibody-based therapies which involve administering of anti-polypeptides and anti-polynucleotide antibodies to a mammalian, preferably human, patient for treating one or more of the described disorders. Methods for producing anti-polypeptides and anti-polynucleotide antibodies polyclonal and monoclonal

antibodies are described in detail elsewhere herein. Such antibodies may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

In particular, the antibodies, fragments and derivatives of the present invention are useful for treating a subject having or developing cell proliferative and/or differentiation disorders as described herein. Such treatment comprises administering a single or multiple doses of the antibody, or a fragment, derivative, or a conjugate thereof.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors, for example., which serve to increase the number or activity of effector cells which interact with the antibodies.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragements thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides, including fragements thereof. Preferred binding affinities include those with a dissociation constant or Kd less than $5X10^{-6}M$, $10^{-6}M$, $5X10^{-7}M$, $10^{-7}M$, $5X10^{-8}M$, $10^{-8}M$, $5X10^{-9}M$, $10^{-9}M$, $5X10^{-10}M$, $10^{-10}M$, $5X10^{-11}M$, $10^{-11}M$, $5X10^{-12}M$, $10^{-12}M$, $5X10^{-13}M$, $10^{-13}M$, $5X10^{-14}M$, $10^{-14}M$, $5X10^{-15}M$, and $10^{-15}M$.

Moreover, polypeptides of the present invention are useful in inhibiting the angiogenesis of proliferative cells or tissues, either alone, as a protein fusion, or in combination with other polypeptides directly or indirectly, as described elsewhere herein. In a most preferred embodiment, said anti-angiogenesis effect may be achieved indirectly, for example, through the inhibition of hematopoietic, tumor-specific cells, such as tumor-associated macrophages (See Joseph IB, et al. J Natl Cancer Inst, 90(21):1648-53 (1998),

which is hereby incorporated by reference). Antibodies directed to polypeptides or polynucleotides of the present invention may also result in inhibition of angiogenesis directly, or indirectly (See Witte L, et al., Cancer Metastasis Rev. 17(2):155-61 (1998), which is hereby incorporated by reference)).

Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a death-domain receptor, such as tumor necrosis factor (TNF) receptor-1, CD95 (Fas/APO-1), TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1 and -2 (See Schulze-Osthoff K, et.al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides may induce apoptosis through other mechanisms, such as in the activation of other proteins which will activate apoptosis, or through stimulating the expression of said proteins, either alone or in combination with small molecule drugs or adjuviants, such as apoptonin, galectins, thioredoxins, antiinflammatory proteins (See for example, Mutat Res 400(1-2):447-55 (1998), Med Hypotheses.50(5):423-33 (1998), Chem Biol Interact. Apr 24;111-112:23-34 (1998), J Mol Med.76(6):402-12 (1998), Int J Tissue React;20(1):3-15 (1998), which are all hereby incorporated by reference).

Polypeptides, including protein fusions to, or fragments thereof, of the present invention are useful in inhibiting the metastasis of proliferative cells or tissues. Inhibition may occur as a direct result of administering polypeptides, or antibodies directed to said polypeptides as described elsewere herein, or indirectly, such as activating the expression of proteins known to inhibit metastasis, for example alpha 4 integrins, (See, e.g., Curr Top Microbiol Immunol 1998;231:125-41, which is hereby incorporated by reference). Such thereapeutic affects of the present invention may be achieved either alone, or in combination with small molecule drugs or adjuvants.

In another embodiment, the invention provides a method of delivering compositions containing the polypeptides of the invention (e.g., compositions containing polypeptides or polypeptide antibodes associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs) to targeted cells expressing the polypeptide of the present invention. Polypeptides or polypeptide antibodes of the invention may be associated with with

heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. Polypeptides, protein fusions to, or fragments thereof, of the present invention are useful in enhancing the immunogenicity and/or antigenicity of proliferating cells or tissues, either directly, such as would occur if the polypeptides of the present invention 'vaccinated' the immune response to respond to proliferative antigens and immunogens, or indirectly, such as in activating the expression of proteins known to enhance the immune response (e.g. chemokines), to said antigens and immunogens.

Cardiovascular Disorders

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, may be used to treat cardiovascular disorders, including peripheral artery disease, such as limb ischemia.

Cardiovascular disorders include cardiovascular abnormalities, such as arterio-arterial fistula, arteriovenous fistula, cerebral arteriovenous malformations, congenital heart defects, pulmonary atresia, and Scimitar Syndrome. Congenital heart defects include aortic coarctation, cor triatriatum, coronary vessel anomalies, crisscross heart, dextrocardia, patent ductus arteriosus, Ebstein's anomaly, Eisenmenger complex, hypoplastic left heart syndrome, levocardia, tetralogy of fallot, transposition of great vessels, double outlet right ventricle, tricuspid atresia, persistent truncus arteriosus, and heart septal defects, such as aortopulmonary septal defect, endocardial cushion defects, Lutembacher's Syndrome, trilogy of Fallot, ventricular heart septal defects.

Cardiovascular disorders also include heart disease, such as arrhythmias, carcinoid heart disease, high cardiac output, low cardiac output, cardiac tamponade, endocarditis (including bacterial), heart aneurysm, cardiac arrest, congestive heart failure, congestive cardiomyopathy, paroxysmal dyspnea, cardiac edema, heart hypertrophy, congestive cardiomyopathy, left ventricular hypertrophy, right ventricular hypertrophy, post-infarction heart rupture, ventricular septal rupture, heart valve diseases, myocardial diseases, myocardial ischemia, pericardial effusion, pericarditis (including constrictive and tuberculous), pneumopericardium, postpericardiotomy syndrome, pulmonary heart disease, rheumatic heart disease, ventricular dysfunction, hyperemia, cardiovascular pregnancy complications, Scimitar Syndrome, cardiovascular syphilis, and cardiovascular tuberculosis.

Arrhythmias include sinus arrhythmia, atrial fibrillation, atrial flutter, bradycardia, extrasystole, Adams-Stokes Syndrome, bundle-branch block, sinoatrial block, long QT syndrome, parasystole, Lown-Ganong-Levine Syndrome, Mahaim-type pre-excitation syndrome, Wolff-Parkinson-White syndrome, sick sinus syndrome, tachycardias, and ventricular fibrillation. Tachycardias include paroxysmal tachycardia, supraventricular tachycardia, accelerated idioventricular rhythm, atrioventricular nodal reentry tachycardia, ectopic atrial tachycardia, ectopic junctional tachycardia, sinoatrial nodal reentry tachycardia, sinus tachycardia, Torsades de Pointes, and ventricular tachycardia.

Heart valve disease include aortic valve insufficiency, aortic valve stenosis, hear murmurs, aortic valve prolapse, mitral valve prolapse, tricuspid valve prolapse, mitral valve insufficiency, mitral valve stenosis, pulmonary atresia, pulmonary valve insufficiency, pulmonary valve stenosis, tricuspid atresia, tricuspid valve insufficiency, and tricuspid valve stenosis.

Myocardial diseases include alcoholic cardiomyopathy, congestive cardiomyopathy, hypertrophic cardiomyopathy, aortic subvalvular stenosis, pulmonary subvalvular stenosis, restrictive cardiomyopathy, Chagas cardiomyopathy, endocardial fibroelastosis, endomyocardial fibrosis, Kearns Syndrome, myocardial reperfusion injury, and myocarditis.

Myocardial ischemias include coronary disease, such as angina pectoris, coronary aneurysm, coronary arteriosclerosis, coronary thrombosis, coronary vasospasm, myocardial infarction and myocardial stunning.

Cardiovascular diseases also include vascular diseases such as aneurysms, angiodysplasia, angiomatosis, bacillary angiomatosis, Hippel-Lindau Disease, Klippel-Trenaunay-Weber Syndrome, Sturge-Weber Syndrome, angioneurotic edema, aortic diseases, Takayasu's Arteritis, aortitis, Leriche's Syndrome, arterial occlusive diseases, arteritis, enarteritis, polyarteritis nodosa, cerebrovascular disorders, diabetic angiopathies, diabetic retinopathy, embolisms, thrombosis, erythromelalgia, hemorrhoids, hepatic veno-occlusive disease, hypertension, hypotension, ischemia, peripheral vascular diseases, phlebitis, pulmonary veno-occlusive disease, Raynaud's disease, CREST syndrome, retinal vein occlusion, Scimitar syndrome, superior vena cava syndrome, telangiectasia, atacia telangiectasia, hereditary hemorrhagic telangiectasia, varicocele, varicose veins, varicose ulcer, vasculitis, and venous insufficiency.

Aneurysms include dissecting aneurysms, false aneurysms, infected aneurysms, ruptured aneurysms, aortic aneurysms, cerebral aneurysms, coronary aneurysms, heart aneurysms, and iliac aneurysms.

Arterial occlusive diseases include arteriosclerosis, intermittent claudication, carotid stenosis, fibromuscular dysplasias, mesenteric vascular occlusion, Moyamoya disease, renal artery obstruction, retinal artery occlusion, and thromboangiitis obliterans.

Cerebrovascular disorders include carotid artery diseases, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformation, cerebral artery diseases, cerebral embolism and thrombosis, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, cerebral hemorrhage, epidural hematoma, subdural hematoma, subaraxhnoid hemorrhage, cerebral infarction, cerebral ischemia (including transient), subclavian steal syndrome, periventricular leukomalacia, vascular headache, cluster headache, migraine, and vertebrobasilar insufficiency.

Embolisms include air embolisms, amniotic fluid embolisms, cholesterol embolisms, blue toe syndrome, fat embolisms, pulmonary embolisms, and thromoboembolisms. Thrombosis include coronary thrombosis, hepatic vein thrombosis, retinal vein occlusion, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, and thrombophlebitis.

Ischemia includes cerebral ischemia, ischemic colitis, compartment syndromes, anterior compartment syndrome, myocardial ischemia, reperfusion injuries, and peripheral limb ischemia. Vasculitis includes aortitis, arteritis, Behcet's Syndrome, Churg-Strauss Syndrome, mucocutaneous lymph node syndrome, thromboangiitis obliterans, hypersensitivity vasculitis, Schoenlein-Henoch purpura, allergic cutaneous vasculitis, and Wegener's granulomatosis.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, are especially effective for the treatment of critical limb ischemia and coronary disease.

Polypeptides may be administered using any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, biolistic injectors, particle accelerators, gelfoam sponge depots, other commercially available depot materials, osmotic pumps, oral or suppositorial solid pharmaceutical formulations, decanting or topical applications during surgery, aerosol delivery. Such methods are known in the art. Polypeptides may be administered as part of a

Therapeutic, described in more detail below. Methods of delivering polynucleotides are described in more detail herein.

Anti-Angiogenesis Activity

The naturally occurring balance between endogenous stimulators and inhibitors of angiogenesis is one in which inhibitory influences predominate. Rastinejad *et al.*, *Cell* *56*:345-355 (1989). In those rare instances in which neovascularization occurs under normal physiological conditions, such as wound healing, organ regeneration, embryonic development, and female reproductive processes, angiogenesis is stringently regulated and spatially and temporally delimited. Under conditions of pathological angiogenesis such as that characterizing solid tumor growth, these regulatory controls fail. Unregulated angiogenesis becomes pathologic and sustains progression of many neoplastic and non-neoplastic diseases. A number of serious diseases are dominated by abnormal neovascularization including solid tumor growth and metastases, arthritis, some types of eye disorders, and psoriasis. See, e.g., reviews by Moses *et al.*, *Biotech.* *9*:630-634 (1991); Folkman *et al.*, *N. Engl. J. Med.*, *333*:1757-1763 (1995); Auerbach *et al.*, *J. Microvasc. Res.* *29*:401-411 (1985); Folkman, Advances in Cancer Research, eds. Klein and Weinhouse, Academic Press, New York, pp. 175-203 (1985); Patz, *Am. J. Opthalmol.* *94*:715-743 (1982); and Folkman *et al.*, Science *221*:719-725 (1983). In a number of pathological conditions, the process of angiogenesis contributes to the disease state. For example, significant data have accumulated which suggest that the growth of solid tumors is dependent on angiogenesis. Folkman and Klagsbrun, *Science* *235*:442-447 (1987).

The polynucleotides encoding a polypeptide of the present invention may be administered along with other polynucleotides encoding an angiogenic protein. Examples of angiogenic proteins include, but are not limited to, acidic and basic fibroblast growth factors, VEGF-1, VEGF-2, VEGF-3, epidermal growth factor alpha and beta, platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor alpha, hepatocyte growth factor, insulin like growth factor, colony stimulating factor, macrophage colony stimulating factor, granulocyte/macrophage colony stimulating factor, and nitric oxide synthase.

The present invention provides for treatment of diseases or disorders associated with neovascularization by administration of the polynucleotides and/or polypeptides of the

invention, as well as agonists or antagonists of the present invention. Malignant and metastatic conditions which can be treated with the polynucleotides and polypeptides, or agonists or antagonists of the invention include, but are not limited to, malignancies, solid tumors, and cancers described herein and otherwise known in the art (for a review of such disorders, see Fishman *et al.*, Medicine, 2d Ed., J. B. Lippincott Co., Philadelphia (1985)).Thus, the present invention provides a method of treating an angiogenesis-related disease and/or disorder, comprising administering to an individual in need thereof a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist of the invention. For example, polynucleotides, polypeptides, antagonists and/or agonists may be utilized in a variety of additional methods in order to therapeutically treat a cancer or tumor. Cancers which may be treated with polynucleotides, polypeptides, antagonists and/or agonists include, but are not limited to solid tumors, including breast, ovarian, prostate, lung, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, thyroid cancer; primary tumors and metastases; melanomas; glioblastoma; Kaposi's sarcoma; leiomyosarcoma; non- small cell lung cancer; colorectal cancer; advanced malignancies; and blood born tumors such as leukemias. For example, polynucleotides, polypeptides, antagonists and/or agonists may be delivered topically, in order to treat cancers such as skin cancer, head and neck tumors, breast tumors, and Kaposi's sarcoma.

Within yet other aspects, polynucleotides, polypeptides, antagonists and/or agonists may be utilized to treat superficial forms of bladder cancer by, for example, intravesical administration. Polynucleotides, polypeptides, antagonists and/or agonists may be delivered directly into the tumor, or near the tumor site, via injection or a catheter. Of course, as the artisan of ordinary skill will appreciate, the appropriate mode of administration will vary according to the cancer to be treated. Other modes of delivery are discussed herein.

Polynucleotides, polypeptides, antagonists and/or agonists may be useful in treating other disorders, besides cancers, which involve angiogenesis. These disorders include, but are not limited to: benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; artheroscleric plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uvietis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid

arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis.

For example, within one aspect of the present invention methods are provided for treating hypertrophic scars and keloids, comprising the step of administering a polynucleotide, polypeptide, antagonist and/or agonist of the invention to a hypertrophic scar or keloid.

Within one embodiment of the present invention polynucleotides, polypeptides, antagonists and/or agonists are directly injected into a hypertrophic scar or keloid, in order to prevent the progression of these lesions. This therapy is of particular value in the prophylactic treatment of conditions which are known to result in the development of hypertrophic scars and keloids (e.g., burns), and is preferably initiated after the proliferative phase has had time to progress (approximately 14 days after the initial injury), but before hypertrophic scar or keloid development. As noted above, the present invention also provides methods for treating neovascular diseases of the eye, including for example, corneal neovascularization, neovascular glaucoma, proliferative diabetic retinopathy, retrolental fibroplasia and macular degeneration.

Moreover, Ocular disorders associated with neovascularization which can be treated with the polynucleotides and polypeptides of the present invention (including agonists and/or antagonists) include, but are not limited to: neovascular glaucoma, diabetic retinopathy, retinoblastoma, retrolental fibroplasia, uveitis, retinopathy of prematurity macular degeneration, corneal graft neovascularization, as well as other eye inflammatory diseases, ocular tumors and diseases associated with choroidal or iris neovascularization. See, e.g., reviews by Waltman *et al., Am. J. Ophthal. 85*:704-710 (1978) and Gartner *et al., Surv. Ophthal. 22*:291-312 (1978).

Thus, within one aspect of the present invention methods are provided for treating neovascular diseases of the eye such as corneal neovascularization (including corneal graft neovascularization), comprising the step of administering to a patient a therapeutically effective amount of a compound (as described above) to the cornea, such that the formation

of blood vessels is inhibited. Briefly, the cornea is a tissue which normally lacks blood vessels. In certain pathological conditions however, capillaries may extend into the cornea from the pericorneal vascular plexus of the limbus. When the cornea becomes vascularized, it also becomes clouded, resulting in a decline in the patient's visual acuity. Visual loss may become complete if the cornea completely opacitates. A wide variety of disorders can result in corneal neovascularization, including for example, corneal infections (e.g., trachoma, herpes simplex keratitis, leishmaniasis and onchocerciasis), immunological processes (e.g., graft rejection and Stevens-Johnson's syndrome), alkali burns, trauma, inflammation (of any cause), toxic and nutritional deficiency states, and as a complication of wearing contact lenses.

Within particularly preferred embodiments of the invention, may be prepared for topical administration in saline (combined with any of the preservatives and antimicrobial agents commonly used in ocular preparations), and administered in eyedrop form. The solution or suspension may be prepared in its pure form and administered several times daily. Alternatively, anti-angiogenic compositions, prepared as described above, may also be administered directly to the cornea. Within preferred embodiments, the anti-angiogenic composition is prepared with a muco-adhesive polymer which binds to cornea. Within further embodiments, the anti-angiogenic factors or anti-angiogenic compositions may be utilized as an adjunct to conventional steroid therapy. Topical therapy may also be useful prophylactically in corneal lesions which are known to have a high probability of inducing an angiogenic response (such as chemical burns). In these instances the treatment, likely in combination with steroids, may be instituted immediately to help prevent subsequent complications.

Within other embodiments, the compounds described above may be injected directly into the corneal stroma by an ophthalmologist under microscopic guidance. The preferred site of injection may vary with the morphology of the individual lesion, but the goal of the administration would be to place the composition at the advancing front of the vasculature (i.e., interspersed between the blood vessels and the normal cornea). In most cases this would involve perilimbic corneal injection to "protect" the cornea from the advancing blood vessels. This method may also be utilized shortly after a corneal insult in order to prophylactically prevent corneal neovascularization. In this situation the material could be injected in the perilimbic cornea interspersed between the corneal lesion and its undesired

potential limbic blood supply. Such methods may also be utilized in a similar fashion to prevent capillary invasion of transplanted corneas. In a sustained-release form injections might only be required 2-3 times per year. A steroid could also be added to the injection solution to reduce inflammation resulting from the injection itself.

Within another aspect of the present invention, methods are provided for treating neovascular glaucoma, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. In one embodiment, the compound may be administered topically to the eye in order to treat early forms of neovascular glaucoma. Within other embodiments, the compound may be implanted by injection into the region of the anterior chamber angle. Within other embodiments, the compound may also be placed in any location such that the compound is continuously released into the aqueous humor. Within another aspect of the present invention, methods are provided for treating proliferative diabetic retinopathy, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eyes, such that the formation of blood vessels is inhibited.

Within particularly preferred embodiments of the invention, proliferative diabetic retinopathy may be treated by injection into the aqueous humor or the vitreous, in order to increase the local concentration of the polynucleotide, polypeptide, antagonist and/or agonist in the retina. Preferably, this treatment should be initiated prior to the acquisition of severe disease requiring photocoagulation.

Within another aspect of the present invention, methods are provided for treating retrolental fibroplasia, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. The compound may be administered topically, via intravitreous injection and/or via intraocular implants.

Additionally, disorders which can be treated with the polynucleotides, polypeptides, agonists and/or agonists include, but are not limited to, hemangioma, arthritis, psoriasis, angiofibroma, atherosclerotic plaques, delayed wound healing, granulations, hemophilic joints, hypertrophic scars, nonunion fractures, Osler-Weber syndrome, pyogenic granuloma, scleroderma, trachoma, and vascular adhesions.

Moreover, disorders and/or states, which can be treated with be treated with the the polynucleotides, polypeptides, agonists and/or agonists include, but are not limited to, solid tumors, blood born tumors such as leukemias, tumor metastasis, Kaposi's sarcoma, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas, rheumatoid arthritis, psoriasis, ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, and uvietis, delayed wound healing, endometriosis, vascluogenesis, granulations, hypertrophic scars (keloids), nonunion fractures, scleroderma, trachoma, vascular adhesions, myocardial angiogenesis, coronary collaterals, cerebral collaterals, arteriovenous malformations, ischemic limb angiogenesis, Osler-Webber Syndrome, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma fibromuscular dysplasia, wound granulation, Crohn's disease, atherosclerosis, birth control agent by preventing vascularization required for embryo implantation controlling menstruation, diseases that have angiogenesis as a pathologic consequence such as cat scratch disease (Rochele minalia quintosa), ulcers (Helicobacter pylori), Bartonellosis and bacillary angiomatosis.

In one aspect of the birth control method, an amount of the compound sufficient to block embryo implantation is administered before or after intercourse and fertilization have occurred, thus providing an effective method of birth control, possibly a "morning after" method. Polynucleotides, polypeptides, agonists and/or agonists may also be used in controlling menstruation or administered as either a peritoneal lavage fluid or for peritoneal implantation in the treatment of endometriosis.

Polynucleotides, polypeptides, agonists and/or agonists of the present invention may be incorporated into surgical sutures in order to prevent stitch granulomas.

Polynucleotides, polypeptides, agonists and/or agonists may be utilized in a wide variety of surgical procedures. For example, within one aspect of the present invention a compositions (in the form of, for example, a spray or film) may be utilized to coat or spray an area prior to removal of a tumor, in order to isolate normal surrounding tissues from malignant tissue, and/or to prevent the spread of disease to surrounding tissues. Within other aspects of the present invention, compositions (e.g., in the form of a spray) may be delivered via endoscopic procedures in order to coat tumors, or inhibit angiogenesis in a desired locale. Within yet other aspects of the present invention, surgical meshes which have been coated

with anti- angiogenic compositions of the present invention may be utilized in any procedure wherein a surgical mesh might be utilized. For example, within one embodiment of the invention a surgical mesh laden with an anti-angiogenic composition may be utilized during abdominal cancer resection surgery (e.g., subsequent to colon resection) in order to provide support to the structure, and to release an amount of the anti-angiogenic factor.

Within further aspects of the present invention, methods are provided for treating tumor excision sites, comprising administering a polynucleotide, polypeptide, agonist and/or agonist to the resection margins of a tumor subsequent to excision, such that the local recurrence of cancer and the formation of new blood vessels at the site is inhibited. Within one embodiment of the invention, the anti-angiogenic compound is administered directly to the tumor excision site (e.g., applied by swabbing, brushing or otherwise coating the resection margins of the tumor with the anti-angiogenic compound). Alternatively, the anti-angiogenic compounds may be incorporated into known surgical pastes prior to administration. Within particularly preferred embodiments of the invention, the anti-angiogenic compounds are applied after hepatic resections for malignancy, and after neurosurgical operations.

Within one aspect of the present invention, polynucleotides, polypeptides, agonists and/or agonists may be administered to the resection margin of a wide variety of tumors, including for example, breast, colon, brain and hepatic tumors. For example, within one embodiment of the invention, anti-angiogenic compounds may be administered to the site of a neurological tumor subsequent to excision, such that the formation of new blood vessels at the site are inhibited.

The polynucleotides, polypeptides, agonists and/or agonists of the present invention may also be administered along with other anti-angiogenic factors. Representative examples of other anti-angiogenic factors include: Anti-Invasive Factor, retinoic acid and derivatives thereof, paclitaxel, Suramin, Tissue Inhibitor of Metalloproteinase-1, Tissue Inhibitor of Metalloproteinase-2, Plasminogen Activator Inhibitor-1, Plasminogen Activator Inhibitor-2, and various forms of the lighter "d group" transition metals.

Lighter "d group" transition metals include, for example, vanadium, molybdenum, tungsten, titanium, niobium, and tantalum species. Such transition metal species may form transition metal complexes. Suitable complexes of the above-mentioned transition metal species include oxo transition metal complexes.

Representative examples of vanadium complexes include oxo vanadium complexes such as vanadate and vanadyl complexes. Suitable vanadate complexes include metavanadate and orthovanadate complexes such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

Representative examples of tungsten and molybdenum complexes also include oxo complexes. Suitable oxo tungsten complexes include tungstate and tungsten oxide complexes. Suitable tungstate complexes include ammonium tungstate, calcium tungstate, sodium tungstate dihydrate, and tungstic acid. Suitable tungsten oxides include tungsten (IV) oxide and tungsten (VI) oxide. Suitable oxo molybdenum complexes include molybdate, molybdenum oxide, and molybdenyl complexes. Suitable molybdate complexes include ammonium molybdate and its hydrates, sodium molybdate and its hydrates, and potassium molybdate and its hydrates. Suitable molybdenum oxides include molybdenum (VI) oxide, molybdenum (VI) oxide, and molybdic acid. Suitable molybdenyl complexes include, for example, molybdenyl acetylacetonate. Other suitable tungsten and molybdenum complexes include hydroxo derivatives derived from, for example, glycerol, tartaric acid, and sugars.

A wide variety of other anti-angiogenic factors may also be utilized within the context of the present invention. Representative examples include platelet factor 4; protamine sulphate; sulphated chitin derivatives (prepared from queen crab shells), (Murata et al., Cancer Res. 51:22-26, 1991); Sulphated Polysaccharide Peptidoglycan Complex (SP- PG) (the function of this compound may be enhanced by the presence of steroids such as estrogen, and tamoxifen citrate); Staurosporine; modulators of matrix metabolism, including for example, proline analogs, cishydroxyproline, d,L-3,4-dehydroproline, Thiaproline, alpha,alpha-dipyridyl, aminopropionitrile fumarate; 4-propyl-5-(4-pyridinyl)-2(3H)-oxazolone; Methotrexate; Mitoxantrone; Heparin; Interferons; 2 Macroglobulin-serum; ChIMP-3 (Pavloff et al., J. Bio. Chem. 267:17321-17326, 1992); Chymostatin (Tomkinson et al., Biochem J. 286:475-480, 1992); Cyclodextrin Tetradecasulfate; Eponemycin; Camptothecin; Fumagillin (Ingber et al., Nature 348:555-557, 1990); Gold Sodium Thiomalate ("GST"; Matsubara and Ziff, J. Clin. Invest. 79:1440-1446, 1987); anticollagenase-serum; alpha2-antiplasmin (Holmes et al., J. Biol. Chem. 262(4):1659-1664, 1987); Bisantrene (National Cancer Institute); Lobenzarit disodium (N-(2)-carboxyphenyl-4-

chloroanthronilic acid disodium or "CCA"; Takeuchi et al., Agents Actions 36:312-316, 1992); Thalidomide; Angostatic steroid; AGM-1470; carboxynaminolmidazole; and metalloproteinase inhibitors such as BB94.

Diseases at the Cellular Level

Diseases associated with increased cell survival or the inhibition of apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as antagonists or agonists of the present invention, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and ovarian cancer); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection. In preferred embodiments, polynucleotides, polypeptides, and/or antagonists of the invention are used to inhibit growth, progression, and/or metasis of cancers, in particular those listed above.

Additional diseases or conditions associated with increased cell survival that could be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's

tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma, and retinoblastoma.

Diseases associated with increased apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, include AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Retinitis pigmentosa, Cerebellar degeneration and brain tumor or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) myelodysplastic syndromes (such as aplastic anemia), graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury), liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestosis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

Wound Healing and Epithelial Cell Proliferation

In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate epithelial cell proliferation and basal keratinocytes for the purpose of wound healing, and to stimulate hair follicle production and healing of dermal wounds. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may be clinically useful in stimulating wound healing including surgical wounds, excisional wounds, deep wounds involving damage of the dermis and epidermis, eye tissue wounds, dental tissue wounds, oral cavity

wounds, diabetic ulcers, dermal ulcers, cubitus ulcers, arterial ulcers, venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associted with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote dermal reestablishment subsequent to dermal loss

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to increase the adherence of skin grafts to a wound bed and to stimulate re-epithelialization from the wound bed. The following are types of grafts that polynucleotides or polypeptides, agonists or antagonists of the present invention, could be used to increase adherence to a wound bed: autografts, artificial skin, allografts, autodermic graft, autoepdermic grafts, avacular grafts, Blair-Brown grafts, bone graft, brephoplastic grafts, cutis graft, delayed graft, dermic graft, epidermic graft, fascia graft, full thickness graft, heterologous graft, xenograft, homologous graft, hyperplastic graft, lamellar graft, mesh graft, mucosal graft, Ollier-Thiersch graft, omenpal graft, patch graft, pedicle graft, penetrating graft, split skin graft, thick split graft. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, can be used to promote skin strength and to improve the appearance of aged skin.

It is believed that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, will also produce changes in hepatocyte proliferation, and epithelial cell proliferation in the lung, breast, pancreas, stomach, small intesting, and large intestine. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could promote proliferation of epithelial cells such as sebocytes, hair follicles, hepatocytes, type II pneumocytes, mucin-producing goblet cells, and other epithelial cells and their progenitors contained within the skin, lung, liver, and gastrointestinal tract. Polynucleotides or polypeptides, agonists or antagonists of the present invention, may promote proliferation of endothelial cells, keratinocytes, and basal keratinocytes.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to reduce the side effects of gut toxicity that result from radiation, chemotherapy treatments or viral infections. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may have a cytoprotective effect on

the small intestine mucosa. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may also stimulate healing of mucositis (mouth ulcers) that result from chemotherapy and viral infections.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could further be used in full regeneration of skin in full and partial thickness skin defects, including burns, (i.e., repopulation of hair follicles, sweat glands, and sebaceous glands), treatment of other skin defects such as psoriasis. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat epidermolysis bullosa, a defect in adherence of the epidermis to the underlying dermis which results in frequent, open and painful blisters by accelerating reepithelialization of these lesions. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to treat gastric and doudenal ulcers and help heal by scar formation of the mucosal lining and regeneration of glandular mucosa and duodenal mucosal lining more rapidly. Inflamamatory bowel diseases, such as Crohn's disease and ulcerative colitis, are diseases which result in destruction of the mucosal surface of the small or large intestine, respectively. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote the resurfacing of the mucosal surface to aid more rapid healing and to prevent progression of inflammatory bowel disease. Treatment with polynucleotides or polypeptides, agonists or antagonists of the present invention, is expected to have a significant effect on the production of mucus throughout the gastrointestinal tract and could be used to protect the intestinal mucosa from injurious substances that are ingested or following surgery. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat diseases associate with the under expression.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to prevent and heal damage to the lungs due to various pathological states. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, which could stimulate proliferation and differentiation and promote the repair of alveoli and brochiolar epithelium to prevent or treat acute or chronic lung damage. For example, emphysema, which results in the progressive loss of aveoli, and inhalation injuries, i.e., resulting from smoke inhalation and burns, that cause necrosis of the bronchiolar epithelium and alveoli could be effectively treated using polynucleotides or

polypeptides, agonists or antagonists of the present invention. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to stimulate the proliferation of and differentiation of type II pneumocytes, which may help treat or prevent disease such as hyaline membrane diseases, such as infant respiratory distress syndrome and bronchopulmonary displasia, in premature infants.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could stimulate the proliferation and differentiation of hepatocytes and, thus, could be used to alleviate or treat liver diseases and pathologies such as fulminant liver failure caused by cirrhosis, liver damage caused by viral hepatitis and toxic substances (i.e., acetaminophen, carbon tetraholoride and other hepatotoxins known in the art).

In addition, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used treat or prevent the onset of diabetes mellitus. In patients with newly diagnosed Types I and II diabetes, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to maintain the islet function so as to alleviate, delay or prevent permanent manifestation of the disease. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used as an auxiliary in islet cell transplantation to improve or promote islet cell function.

<u>Neurological Diseases</u>

In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate neurological cell proliferation and/or differentiation. Therefore, polynucleotides, polypeptides, agonists and/or antagonists of the invention may be used to treat and/or detect neurologic diseases. Moreover, polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used as a marker or detector of a particular nervous system disease or disorder.

Examples of neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include brain diseases, such as metabolic brain diseases which includes phenylketonuria such as maternal phenylketonuria, pyruvate carboxylase deficiency, pyruvate dehydrogenase complex deficiency, Wernicke's Encephalopathy, brain edema, brain neoplasms such as

cerebellar neoplasms which include infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms, supratentorial neoplasms, canavan disease, cerebellar diseases such as cerebellar ataxia which include spinocerebellar degeneration such as ataxia telangiectasia, cerebellar dyssynergia, Friederich's Ataxia, Machado-Joseph Disease, olivopontocerebellar atrophy, cerebellar neoplasms such as infratentorial neoplasms, diffuse cerebral sclerosis such as encephalitis periaxialis, globoid cell leukodystrophy, metachromatic leukodystrophy and subacute sclerosing panencephalitis, cerebrovascular disorders (such as carotid artery diseases which include carotid artery thrombosis, carotid stenosis and Moyamoya Disease, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformations, cerebral artery diseases, cerebral embolism and thrombosis such as carotid artery thrombosis, sinus thrombosis and Wallenberg's Syndrome, cerebral hemorrhage such as epidural hematoma, subdural hematoma and subarachnoid hemorrhage, cerebral infarction, cerebral ischemia such as transient cerebral ischemia, Subclavian Steal Syndrome and vertebrobasilar insufficiency, vascular dementia such as multi-infarct dementia, periventricular leukomalacia, vascular headache such as cluster headache, migraine, dementia such as AIDS Dementia Complex, presenile dementia such as Alzheimer's Disease and Creutzfeldt-Jakob Syndrome, senile dementia such as Alzheimer's Disease and progressive supranuclear palsy, vascular dementia such as multi-infarct dementia, encephalitis which include encephalitis periaxialis, viral encephalitis such as epidemic encephalitis, Japanese Encephalitis, St. Louis Encephalitis, tick-borne encephalitis and West Nile Fever, acute disseminated encephalomyelitis, meningoencephalitis such as uveomeningoencephalitic syndrome, Postencephalitic Parkinson Disease and subacute sclerosing panencephalitis, encephalomalacia such as periventricular leukomalacia, epilepsy such as generalized epilepsy which includes infantile spasms, absence epilepsy, myoclonic epilepsy which includes MERRF Syndrome, tonic-clonic epilepsy, partial epilepsy such as complex partial epilepsy, frontal lobe epilepsy and temporal lobe epilepsy, post-traumatic epilepsy, status epilepticus such as Epilepsia Partialis Continua, Hallervorden-Spatz Syndrome, hydrocephalus such as Dandy-Walker Syndrome and normal pressure hydrocephalus, hypothalamic diseases such as hypothalamic neoplasms, cerebral malaria, narcolepsy which includes cataplexy, bulbar poliomyelitis, cerebri pseudotumor, Rett Syndrome, Reye's Syndrome, thalamic diseases, cerebral toxoplasmosis, intracranial tuberculoma and Zellweger Syndrome, central nervous

system infections such as AIDS Dementia Complex, Brain Abscess, subdural empyema, encephalomyelitis such as Equine Encephalomyelitis, Venezuelan Equine Encephalomyelitis, Necrotizing Hemorrhagic Encephalomyelitis, Visna, cerebral malaria, meningitis such as arachnoiditis, aseptic meningtitis such as viral meningtitis which includes lymphocytic choriomeningitis. Bacterial meningtitis which includes Haemophilus Meningtitis, Listeria Meningtitis, Meningococcal Meningtitis such as Waterhouse-Friderichsen Syndrome, Pneumococcal Meningtitis and meningeal tuberculosis, fungal meningitis such as Cryptococcal Meningtitis, subdural effusion, meningoencephalitis such as uvemeningoencephalitic syndrome, myelitis such as transverse myelitis, neurosyphilis such as tabes dorsalis, poliomyelitis which includes bulbar poliomyelitis and postpoliomyelitis syndrome, prion diseases (such as Creutzfeldt-Jakob Syndrome, Bovine Spongiform Encephalopathy, Gerstmann-Straussler Syndrome, Kuru, Scrapie) cerebral toxoplasmosis, central nervous system neoplasms such as brain neoplasms that include cerebellear neoplasms such as infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms and supratentorial neoplasms, meningeal neoplasms, spinal cord neoplasms which include epidural neoplasms, demyelinating diseases such as Canavan Diseases, diffuse cerebral sceloris which includes adrenoleukodystrophy, encephalitis periaxialis, globoid cell leukodystrophy, diffuse cerebral sclerosis such as metachromatic leukodystrophy, allergic encephalomyelitis, necrotizing hemorrhagic encephalomyelitis, progressive multifocal leukoencephalopathy, multiple sclerosis, central pontine myelinolysis, transverse myelitis, neuromyelitis optica, Scrapie, Swayback, Chronic Fatigue Syndrome, Visna, High Pressure Nervous Syndrome, Meningism, spinal cord diseases such as amyotonia congenita, amyotrophic lateral sclerosis, spinal muscular atrophy such as Werdnig-Hoffmann Disease, spinal cord compression, spinal cord neoplasms such as epidural neoplasms, syringomyelia, Tabes Dorsalis, Stiff-Man Syndrome, mental retardation such as Angelman Syndrome, Cri-du-Chat Syndrome, De Lange's Syndrome, Down Syndrome, Gangliosidoses such as gangliosidoses G(M1), Sandhoff Disease, Tay-Sachs Disease, Hartnup Disease, homocystinuria, Laurence-Moon- Biedl Syndrome, Lesch-Nyhan Syndrome, Maple Syrup Urine Disease, mucolipidosis such as fucosidosis, neuronal ceroid-lipofuscinosis, oculocerebrorenal syndrome, phenylketonuria such as maternal phenylketonuria, Prader-Willi Syndrome, Rett Syndrome, Rubinstein-Taybi Syndrome, Tuberous Sclerosis, WAGR Syndrome, nervous system abnormalities such as

holoprosencephaly, neural tube defects such as anencephaly which includes hydrangencephaly, Arnold-Chairi Deformity, encephalocele, meningocele, meningomyelocele, spinal dysraphism such as spina bifida cystica and spina bifida occulta, hereditary motor and sensory neuropathies which include Charcot-Marie Disease, Hereditary optic atrophy, Refsum's Disease, hereditary spastic paraplegia, Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies such as Congenital Analgesia and Familial Dysautonomia, Neurologic manifestations (such as agnosia that include Gerstmann's Syndrome, Amnesia such as retrograde amnesia, apraxia, neurogenic bladder, cataplexy, communicative disorders such as hearing disorders that includes deafness, partial hearing loss, loudness recruitment and tinnitus, language disorders such as aphasia which include agraphia, anomia, broca aphasia, and Wernicke Aphasia, Dyslexia such as Acquired Dyslexia, language development disorders, speech disorders such as aphasia which includes anomia, broca aphasia and Wernicke Aphasia, articulation disorders, communicative disorders such as speech disorders which include dysarthria, echolalia, mutism and stuttering, voice disorders such as aphonia and hoarseness, decerebrate state, delirium, fasciculation, hallucinations, meningism, movement disorders such as angelman syndrome, ataxia, athetosis, chorea, dystonia, hypokinesia, muscle hypotonia, myoclonus, tic, torticollis and tremor, muscle hypertonia such as muscle rigidity such as stiff-man syndrome, muscle spasticity, paralysis such as facial paralysis which includes Herpes Zoster Oticus, Gastroparesis, Hemiplegia, ophthalmoplegia such as diplopia, Duane's Syndrome, Horner's Syndrome, Chronic progressive external ophthalmoplegia such as Kearns Syndrome, Bulbar Paralysis, Tropical Spastic Paraparesis, Paraplegia such as Brown-Sequard Syndrome, quadriplegia, respiratory paralysis and vocal cord paralysis, paresis, phantom limb, taste disorders such as ageusia and dysgeusia, vision disorders such as amblyopia, blindness, color vision defects, diplopia, hemianopsia, scotoma and subnormal vision, sleep disorders such as hypersomnia which includes Kleine-Levin Syndrome, insomnia, and somnambulism, spasm such as trismus, unconsciousness such as coma, persistent vegetative state and syncope and vertigo, neuromuscular diseases such as amyotonia congenita, amyotrophic lateral sclerosis, Lambert-Eaton Myasthenic Syndrome, motor neuron disease, muscular atrophy such as spinal muscular atrophy, Charcot-Marie Disease and Werdnig-Hoffmann Disease, Postpoliomyelitis Syndrome, Muscular Dystrophy, Myasthenia Gravis, Myotonia Atrophica, Myotonia Confenita, Nemaline Myopathy, Familial Periodic Paralysis, Multiplex

Paramyloclonus, Tropical Spastic Paraparesis and Stiff-Man Syndrome, peripheral nervous system diseases such as acrodynia, amyloid neuropathies, autonomic nervous system diseases such as Adie's Syndrome, Barre-Lieou Syndrome, Familial Dysautonomia, Horner's Syndrome, Reflex Sympathetic Dystrophy and Shy-Drager Syndrome, Cranial Nerve Diseases such as Acoustic Nerve Diseases such as Acoustic Neuroma which includes Neurofibromatosis 2, Facial Nerve Diseases such as Facial Neuralgia,Melkersson-Rosenthal Syndrome, ocular motility disorders which includes amblyopia, nystagmus, oculomotor nerve paralysis, ophthalmoplegia such as Duane's Syndrome, Horner's Syndrome, Chronic Progressive External Ophthalmoplegia which includes Kearns Syndrome, Strabismus such as Esotropia and Exotropia, Oculomotor Nerve Paralysis, Optic Nerve Diseases such as Optic Atrophy which includes Hereditary Optic Atrophy, Optic Disk Drusen, Optic Neuritis such as Neuromyelitis Optica, Papilledema, Trigeminal Neuralgia, Vocal Cord Paralysis, Demyelinating Diseases such as Neuromyelitis Optica and Swayback, Diabetic neuropathies such as diabetic foot, nerve compression syndromes such as carpal tunnel syndrome, tarsal tunnel syndrome, thoracic outlet syndrome such as cervical rib syndrome, ulnar nerve compression syndrome, neuralgia such as causalgia, cervico-brachial neuralgia, facial neuralgia and trigeminal neuralgia, neuritis such as experimental allergic neuritis, optic neuritis, polyneuritis, polyradiculoneuritis and radiculities such as polyradiculitis, hereditary motor and sensory neuropathies such as Charcot-Marie Disease, Hereditary Optic Atrophy, Refsum's Disease, Hereditary Spastic Paraplegia and Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies which include Congenital Analgesia and Familial Dysautonomia, POEMS Syndrome, Sciatica, Gustatory Sweating and Tetany).

__Infectious Disease__

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention. Examples of viruses, include, but are not limited to Examples of viruses, include, but are not limited to the following DNA and RNA viruses and viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Dengue, EBV, HIV, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza A, Influenza B, and parainfluenza), Papiloma virus, Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiollitis, respiratory syncytial virus, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), Japanese B encephalitis, Junin, Chikungunya, Rift Valley fever, yellow fever, meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat: meningitis, Dengue, EBV, and/or hepatitis (e.g., hepatitis B). In an additional specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat patients nonresponsive to one or more other commercially available hepatitis vaccines. In a further specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat AIDS.

Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, include, but not limited to, the following Gram-Negative and Gram-positive bacteria and bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Cryptococcus neoformans, Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia

(e.g., Borrelia burgdorferi, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, E. coli (e.g., Enterotoxigenic E. coli and Enterohemorrhagic E. coli), Enterobacteriaceae (Klebsiella, Salmonella (e.g., Salmonella typhi, and Salmonella paratyphi), Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Mycobacterium leprae, Vibrio cholerae, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Menigococcal), Meisseria meningitidis, Pasteurellacea Infections (e.g., Actinobacillus, Heamophilus (e.g., Heamophilus influenza type B), Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, Shigella spp., Staphylococcal, Meningiococcal, Pneumococcal and Streptococcal (e.g., Streptococcus pneumoniae and Group B Streptococcus). These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis (e.g., mengitis types A and B), Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. Polynucleotides or polypeptides, agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, Ppolynucleotides, polypeptides, agonists or antagonists of the invention are used to treat: tetanus, Diptheria, botulism, and/or meningitis type B.

Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, the following families or class: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas and Sporozoans (e.g., Plasmodium virax, Plasmodium falciparium, Plasmodium malariae and Plasmodium ovale). These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic

infections (e.g., AIDS related), malaria, pregnancy complications, and toxoplasmosis. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

__Regeneration__

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteocarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vasculature (including vascular and lymphatics), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue regeneration of non-healing wounds includes pressure ulcers, ulcers associatedwith vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stoke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotides or polypeptides, as well as agonists or antagonists of the present invention.

<u>Chemotaxis</u>

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may have chemotaxis activity. A chemotaxic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may increase chemotaxic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotaxic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could be used as an inhibitor of chemotaxis.

<u>Binding Activity</u>

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit (antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors),or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide. Preferred cells include cells from mammals, yeast, Drosophila, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

Additionally, the receptor to which the polypeptide of the present invention binds can be identified by numerous methods known to those of skill in the art, for example, ligand

panning and FACS sorting (Coligan, et al., Current Protocols in Immun., 1(2), Chapter 5, (1991)). For example, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the polypeptides, for example, NIH3T3 cells which are known to contain multiple receptors for the FGF family proteins, and SC-3 cells, and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the polypeptides. Transfected cells which are grown on glass slides are exposed to the polypeptide of the present invention, after they have been labelled. The polypeptides can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase.

Following fixation and incubation, the slides are subjected to auto-radiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an iterative sub-pooling and re-screening process, eventually yielding a single clones that encodes the putative receptor.

As an alternative approach for receptor identification, the labeled polypeptides can be photoaffinity linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE analysis and exposed to X-ray film. The labeled complex containing the receptors of the polypeptides can be excised, resolved into peptide fragments, and subjected to protein microsequencing. The amino acid sequence obtained from microsequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the genes encoding the putative receptors.

Moreover, the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling") may be employed to modulate the activities of the polypeptide of the present invention thereby effectively generating agonists and antagonists of the polypeptide of the present invention. *See generally*, U.S. Patent Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458, and Patten, P. A., *et al., Curr. Opinion Biotechnol.* 8:724-33 (1997); Harayama, S. *Trends Biotechnol.* 16(2):76-82 (1998); Hansson, L. O., *et al., J. Mol. Biol.* 287:265-76 (1999); and Lorenzo, M. M. and Blasco, R. *Biotechniques* 24(2):308-13 (1998) (each of these patents and publications are hereby incorporated by reference). In one embodiment, alteration of polynucleotides and corresponding polypeptides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments into a desired molecule by homologous, or site-specific, recombination. In another embodiment, polynucleotides and corresponding

polypeptides may be alterred by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of the polypeptide of the present invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules. In preferred embodiments, the heterologous molecules are family members. In further preferred embodiments, the heterologous molecule is a growth factor such as, for example, platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I), transforming growth factor (TGF)-alpha, epidermal growth factor (EGF), fibroblast growth factor (FGF), TGF-beta, bone morphogenetic protein (BMP)-2, BMP-4, BMP-5, BMP-6, BMP-7, activins A and B, decapentaplegic(dpp), 60A, OP-2, dorsalin, growth differentiation factors (GDFs), nodal, MIS, inhibin-alpha, TGF-beta1, TGF-beta2, TGF-beta3, TGF-beta5, and glial-derived neurotrophic factor (GDNF).

Other preferred fragments are biologically active fragments of the polypeptide of the present invention. Biologically active fragments are those exhibiting activity similár, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Additionally, this invention provides a method of screening compounds to identify those which modulate the action of the polypeptide of the present invention. An example of such an assay comprises combining a mammalian fibroblast cell, a the polypeptide of the present invention, the compound to be screened and ^{3}[H] thymidine under cell culture conditions where the fibroblast cell would normally proliferate. A control assay may be performed in the absence of the compound to be screened and compared to the amount of fibroblast proliferation in the presence of the compound to determine if the compound stimulates proliferation by determining the uptake of ^{3}[H] thymidine in each case. The amount of fibroblast cell proliferation is measured by liquid scintillation chromatography which measures the incorporation of ^{3}[H] thymidine. Both agonist and antagonist compounds may be identified by this procedure.

In another method, a mammalian cell or membrane preparation expressing a receptor for a polypeptide of the present invention is incubated with a labeled polypeptide of the

present invention in the presence of the compound. The ability of the compound to enhance or block this interaction could then be measured. Alternatively, the response of a known second messenger system following interaction of a compound to be screened and the receptor is measured and the ability of the compound to bind to the receptor and elicit a second messenger response is measured to determine if the compound is a potential agonist or antagonist. Such second messenger systems include but are not limited to, cAMP guanylate cyclase, ion channels or phosphoinositide hydrolysis.

All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptides of the invention from suitably manipulated cells or tissues.

Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the present invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the present invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

Targeted Delivery

In another embodiment, the invention provides a method of delivering compositions to targeted cells expressing a receptor for a polypeptide of the invention, or cells expressing a cell bound form of a polypeptide of the invention.

As discussed herein, polypeptides or antibodies of the invention may be associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (including antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method

for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention (e.g., polypeptides of the invention or antibodies of the invention) in association with toxins or cytotoxic prodrugs.

By "toxin" is meant compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNAse, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. By "cytotoxic prodrug" is meant a non-toxic compound that is converted by an enzyme, normally present in the cell, into a cytotoxic compound. Cytotoxic prodrugs that may be used according to the methods of the invention include, but are not limited to, glutamyl derivatives of benzoic acid mustard alkylating agent, phosphate derivatives of etoposide or mitomycin C, cytosine arabinoside, daunorubisin, and phenoxyacetamide derivatives of doxorubicin.

Drug Screening

Further contemplated is the use of the polypeptides of the present invention, or the polynucleotides encoding these polypeptides, to screen for molecules which modify the activities of the polypeptides of the present invention. Such a method would include contacting the polypeptide of the present invention with a selected compound(s) suspected of having antagonist or agonist activity, and assaying the activity of these polypeptides following binding.

This invention is particularly useful for screening therapeutic compounds by using the

polypeptides of the present invention, or binding fragments thereof, in any of a variety of drug screening techniques. The polypeptide or fragment employed in such a test may be affixed to a solid support, expressed on a cell surface, free in solution, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. One may measure, for example, the formulation of complexes between the agent being tested and a polypeptide of the present invention.

Thus, the present invention provides methods of screening for drugs or any other agents which affect activities mediated by the polypeptides of the present invention. These methods comprise contacting such an agent with a polypeptide of the present invention or a fragment thereof and assaying for the presence of a complex between the agent and the polypeptide or a fragment thereof, by methods well known in the art. In such a competitive binding assay, the agents to screen are typically labeled. Following incubation, free agent is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of a particular agent to bind to the polypeptides of the present invention.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to the polypeptides of the present invention, and is described in great detail in European Patent Application 84/03564, published on September 13, 1984, which is incorporated herein by reference herein. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with polypeptides of the present invention and washed. Bound polypeptides are then detected by methods well known in the art. Purified polypeptides are coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies may be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding polypeptides of the present invention specifically compete with a test compound for binding to the polypeptides or fragments thereof. In this manner, the antibodies are used to detect the presence of any peptide which shares one or more antigenic epitopes with a polypeptide of the invention.

Antisense And Ribozvme (Antagonists)

In specific embodiments, antagonists according to the present invention are nucleic acids corresponding to the sequences contained in SEQ ID NO:X, or the complementary strand thereof, and/or to nucleotide sequences contained in the cDNA contained in the related cDNA clone identified in Table 1. In one embodiment, antisense sequence is generated internally, by the organism, in another embodiment, the antisense sequence is separately administered (see, for example, O'Connor, J., Neurochem. 56:560 (1991). Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Antisense technology can be used to control gene expression through antisense DNA or RNA, or through triple-helix formation. Antisense techniques are discussed for example, in Okano, J., Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance, Lee et al., Nucleic Acids Research 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1300 (1991). The methods are based on binding of a polynucleotide to a complementary DNA or RNA.

For example, the use of c-myc and c-myb antisense RNA constructs to inhibit the growth of the non-lymphocytic leukemia cell line HL-60 and other cell lines was previously described. (Wickstrom et al. (1988); Anfossi et al. (1989)). These experiments were performed in vitro by incubating cells with the oligoribonucleotide. A similar procedure for in vivo use is described in WO 91/15580. Briefly, a pair of oligonucleotides for a given antisense RNA is produced as follows: A sequence complimentary to the first 15 bases of the open reading frame is flanked by an EcoR1 site on the 5 end and a HindIII site on the 3 end. Next, the pair of oligonucleotides is heated at 90°C for one minute and then annealed in 2X ligation buffer (20mM TRIS HCl pH 7.5, 10mM MgCl2, 10MM dithiothreitol (DTT) and 0.2 mM ATP) and then ligated to the EcoR1/Hind III site of the retroviral vector PMV7 (WO 91/15580).

For example, the 5' coding portion of a polynucleotide that encodes the polypeptide of the present invention may be used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription thereby preventing transcription and the

production of the receptor. The antisense RNA oligonucleotide hybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into receptor polypeptide.

In one embodiment, the antisense nucleic acid of the invention is produced intracellularly by transcription from an exogenous sequence. For example, a vector or a portion thereof, is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the antisense nucleic acid. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art, used for replication and expression in vertebrate cells. Expression of the sequence encoding the polypeptide of the present invnetion or fragments thereof, can be by any promoter known in the art to act in vertebrate, preferably human cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, Nature 29:304-310 (1981), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., Cell 22:787-797 (1980), the herpes thymidine promoter (Wagner et al., Proc. Natl. Acad. Sci. U.S.A. 78:1441-1445 (1981), the regulatory sequences of the metallothionein gene (Brinster, et al., Nature 296:39-42 (1982)), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a gene of the present invention. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the larger the hybridizing nucleic acid, the more base mismatches with a RNA it may contain and still form a stable duplex (or triplex as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

Oligonucleotides that are complementary to the 5' end of the message, e.g., the 5' untranslated sequence up to and including the AUG initiation codon, should work most

efficiently at inhibiting translation. However, sequences complementary to the 3' untranslated sequences of mRNAs have been shown to be effective at inhibiting translation of mRNAs as well. See generally, Wagner, R., 1994, Nature 372:333-335. Thus, oligonucleotides complementary to either the 5'- or 3'- non- translated, non-coding regions of polynucleotide sequences described herein could be used in an antisense approach to inhibit translation of endogenous mRNA. Oligonucleotides complementary to the 5' untranslated region of the mRNA should include the complement of the AUG start codon. Antisense oligonucleotides complementary to mRNA coding regions are less efficient inhibitors of translation but could be used in accordance with the invention. Whether designed to hybridize to the 5'-, 3'- or coding region of mRNA of the present invention, antisense nucleic acids should be at least six nucleotides in length, and are preferably oligonucleotides ranging from 6 to about 50 nucleotides in length. In specific aspects the oligonucleotide is at least 10 nucleotides, at least 17 nucleotides, at least 25 nucleotides or at least 50 nucleotides.

The polynucleotides of the invention can be DNA or RNA or chimeric mixtures or derivatives or modified versions thereof, single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone, for example, to improve stability of the molecule, hybridization, etc. The oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors in vivo), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. U.S.A. 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. 84:648-652; PCT Publication No. WO88/09810, published December 15, 1988) or the blood-brain barrier (see, e.g., PCT Publication No. WO89/10134, published April 25, 1988), hybridization-triggered cleavage agents. (See, e.g., Krol et al., 1988, BioTechniques 6:958-976) or intercalating agents. (See, e.g., Zon, 1988, Pharm. Res. 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

The antisense oligonucleotide may comprise at least one modified base moiety which is selected from the group including, but not limited to, 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine,

2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

The antisense oligonucleotide may also comprise at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the antisense oligonucleotide comprises at least one modified phosphate backbone selected from the group including, but not limited to, a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal or analog thereof.

In yet another embodiment, the antisense oligonucleotide is an a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual b-units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641). The oligonucleotide is a 2'-0-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analogue (Inoue et al., 1987, FEBS Lett. 215:327-330).

Polynucleotides of the invention may be synthesized by standard methods known in the art, e.g. by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligonucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. U.S.A. 85:7448-7451), etc.

While antisense nucleotides complementary to the coding region sequence could be used, those complementary to the transcribed untranslated region are most preferred.

Potential antagonists according to the invention also include catalytic RNA, or a ribozyme (See, e.g., PCT International Publication WO 90/11364, published October 4, 1990; Sarver et al, Science 247:1222-1225 (1990). While ribozymes that cleave mRNA at

site specific recognition sequences can be used to destroy mRNAs, the use of hammerhead ribozymes is preferred. Hammerhead ribozymes cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The sole requirement is that the target mRNA have the following sequence of two bases: 5'-UG-3'. The construction and production of hammerhead ribozymes is well known in the art and is described more fully in Haseloff and Gerlach, Nature 334:585-591 (1988). There are numerous potential hammerhead ribozyme cleavage sites within the nucleotide sequence of SEQ ID NO:X. Preferably, the ribozyme is engineered so that the cleavage recognition site is located near the 5' end of the mRNA; i.e., to increase efficiency and minimize the intracellular accumulation of non-functional mRNA transcripts.

As in the antisense approach, the ribozymes of the invention can be composed of modified oligonucleotides (e.g. for improved stability, targeting, etc.) and should be delivered to cells which express in vivo. DNA constructs encoding the ribozyme may be introduced into the cell in the same manner as described above for the introduction of antisense encoding DNA. A preferred method of delivery involves using a DNA construct "encoding" the ribozyme under the control of a strong constitutive promoter, such as, for example, pol III or pol II promoter, so that transfected cells will produce sufficient quantities of the ribozyme to destroy endogenous messages and inhibit translation. Since ribozymes unlike antisense molecules, are catalytic, a lower intracellular concentration is required for efficiency.

Antagonist/agonist compounds may be employed to inhibit the cell growth and proliferation effects of the polypeptides of the present invention on neoplastic cells and tissues, i.e. stimulation of angiogenesis of tumors, and, therefore, retard or prevent abnormal cellular growth and proliferation, for example, in tumor formation or growth.

The antagonist/agonist may also be employed to prevent hyper-vascular diseases, and prevent the proliferation of epithelial lens cells after extracapsular cataract surgery. Prevention of the mitogenic activity of the polypeptides of the present invention may also be desirous in cases such as restenosis after balloon angioplasty.

The antagonist/agonist may also be employed to prevent the growth of scar tissue during wound healing.

The antagonist/agonist may also be employed to treat the diseases described herein.

Thus, the invention provides a method of treating disorders or diseases, including but not limited to the disorders or diseases listed throughout this application, associated with

overexpression of a polynucleotide of the present invention by administering to a patient (a) an antisense molecule directed to the polynucleotide of the present invention, and/or (b) a ribozyme directed to the polynucleotide of the present invention.

__Other Activities__

A polypeptide, polynucleotide, agonist, or antagonist of the present invention, as a result of the ability to stimulate vascular endothelial cell growth, may be employed in treatment for stimulating re-vascularization of ischemic tissues due to various disease conditions such as thrombosis, arteriosclerosis, and other cardiovascular conditions. The polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to stimulate angiogenesis and limb regeneration, as discussed above.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for treating wounds due to injuries, burns, post-operative tissue repair, and ulcers since they are mitogenic to various cells of different origins, such as fibroblast cells and skeletal muscle cells, and therefore, facilitate the repair or replacement of damaged or diseased tissue.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed stimulate neuronal growth and to treat and prevent neuronal damage which occurs in certain neuronal disorders or neuro-degenerative conditions such as Alzheimer's disease, Parkinson's disease, and AIDS-related complex. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may have the ability to stimulate chondrocyte growth, therefore, they may be employed to enhance bone and periodontal regeneration and aid in tissue transplants or bone grafts.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be also be employed to prevent skin aging due to sunburn by stimulating keratinocyte growth.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for preventing hair loss, since FGF family members activate hair-forming cells and promotes melanocyte growth. Along the same lines, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be employed to stimulate growth and differentiation of hematopoietic cells and bone marrow cells when used in combination with other cytokines.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to maintain organs before transplantation or for supporting cell culture of primary tissues. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for inducing tissue of mesodermal origin to differentiate in early embryos.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, caricadic rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

The above-recited applications have uses in a wide variety of hosts. Such hosts include, but are not limited to, human, murine, rabbit, goat, guinea pig, camel, horse, mouse, rat, hamster, pig, micro-pig, chicken, goat, cow, sheep, dog, cat, non-human primate, and human. In specific embodiments, the host is a mouse, rabbit, goat, guinea pig, chicken, rat, hamster, pig, sheep, dog or cat. In preferred embodiments, the host is a mammal. In most preferred embodiments, the host is a human.

Other Preferred Embodiments

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which comprises a cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of an open reading frame sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a

nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleotide sequence of SEQ ID NO:X; or the cDNA in the related cDNA clone identified in Table 1 which encodes a protein, wherein the method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence of the cDNA in the related cDNA clone contained in the deposit.

Also preferred is the above method for diagnosing a pathological condition which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the

group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a DNA microarray or "chip" of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, 50, 100, 150, 200, 250, 300, 500, 1000, 2000, 3000 or 4000 nucleotide sequences, wherein at least one sequence in said DNA microarray or "chip" is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the cDNA clone referenced in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a portion of said polypeptide encoded by the cDNA clone referenced in Table 1; a polypeptide encoded by SEQ ID NO:X; and/or the polypeptide sequence of SEQ ID NO:Y.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in

a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleic acid sequence identified in Table 1 encoding a polypeptide, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of:

polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a human protein comprising an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a protein activity, which method comprises administering to such an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to increase the level of said protein activity in said individual.

Also preferred is a method of treatment of an individual in need of a decreased level of a protein activity, which method comprised administering to such an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to decrease the level of said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

Examples

Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample

Each deposited cDNA clone is contained in a plasmid vector. Table 5 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The following correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 5 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

Vector Used to Construct Library	Corresponding Deposited Plasmid
Lambda Zap	pBluescript (pBS)
Uni-Zap XR	pBluescript (pBS)
Zap Express	pBK
lafmid BA	plafmid BA
pSport1	pSport1
pCMVSport 2.0	pCMVSport 2.0
pCMVSport 3.0	pCMVSport 3.0
pCR®2.1	pCR®2.1

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS. The S and K refers to the orientation of the polylinker to the T7 and T3

primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR®2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 5, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited by reference to Table 2 and 5 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone referenced in Table 1.

TABLE 5

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HUKA HUKB HUKC HUKD HUKE HUKF HUKG	Human Uterine Cancer	Lambda ZAP II	LP01
HCNA HCNB	Human Colon	Lambda Zap II	LP01
HFFA	Human Fetal Brain, random primed	Lambda Zap II	LP01
HTWA	Resting T-Cell	Lambda ZAP II	LP01
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP01
HLMB HLMF HLMG HLMH HLMI HLMJ HLMM HLMN	breast lymph node CDNA library	Lambda ZAP II	LP01
HCQA HCQB	human colon cancer	Lamda ZAP II	LP01
HMEA HMEC HMED HMEE HMEF HMEG HMEI HMEJ HMEK HMEL	Human Microvascular Endothelial Cells, fract. A	Lambda ZAP II	LP01
HUSA HUSC	Human Umbilical Vein Endothelial Cells, fract. A	Lambda ZAP II	LP01
HLQA HLQB	Hepatocellular Tumor	Lambda ZAP II	LP01
HHGA HHGB HHGC HHGD	Hemangiopericytoma	Lambda ZAP II	LP01
HSDM	Human Striatum Depression, re-rescue	Lambda ZAP II	LP01
HUSH	H Umbilical Vein Endothelial Cells, frac A, re-excision	Lambda ZAP II	LP01
HSGS	Salivary gland, subtracted	Lambda ZAP II	LP01
HFXA HFXB HFXC HFXD HFXE HFXF HFXG HFXH	Brain frontal cortex	Lambda ZAP II	LP01
HPQA HPQB HPQC	PERM TF274	Lambda ZAP II	LP01
HFXJ HFXK	Brain Frontal Cortex, re-excision	Lambda ZAP II	LP01
HCWA HCWB HCWC HCWD HCWE HCWF HCWG HCWH HCWI HCWJ HCWK	CD34 positive cells (Cord Blood)	ZAP Express	LP02
HCUA HCUB HCUC	CD34 depleted Buffy Coat (Cord Blood)	ZAP Express	LP02
HRSM	A-14 cell line	ZAP Express	LP02
HRSA	A1-CELL LINE	ZAP Express	LP02
HCUD HCUE HCUF HCUG HCUH HCUI	CD34 depleted Buffy Coat (Cord Blood), re-excision	ZAP Express	LP02
HBXE HBXF HBXG	H. Whole Brain #2, re-excision	ZAP Express	LP02
HRLM	L8 cell line	ZAP Express	LP02
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP02
HUDA HUDB HUDC	Testes	ZAP Express	LP02
HHTM HHTN HHTO	H. hypothalamus, frac A;re-excision	ZAP Express	LP02
HHTL	H. hypothalamus, frac A	ZAP Express	LP02
HASA HASD	Human Adult Spleen	Uni-ZAP XR	LP03
HFKC HFKD HFKE HFKF HFKG	Human Fetal Kidney	Uni-ZAP XR	LP03
HE8A HE8B HE8C HE8D HE8E HE8F HE8M HE8N	Human 8 Week Whole Embryo	Uni-ZAP XR	LP03
HGBA HGBD HGBE HGBF HGBG HGBH HGBI	Human Gall Bladder	Uni-ZAP XR	LP03
HLHA HLHB HLHC HLHD HLHE HLHF HLHG HLHH HLHQ	Human Fetal Lung III	Uni-ZAP XR	LP03
HPMA HPMB HPMC HPMD HPME HPMF HPMG HPMH	Human Placenta	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP03
HSIA HSIC HSID HSIE	Human Adult Small Intestine	Uni-ZAP XR	LP03
HTEA HTEB HTEC HTED HTEE HTEF HTEG HTEH HTEI HTEJ HTEK	Human Testes	Uni-ZAP XR	LP03
HTPA HTPB HTPC HTPD HTPE	Human Pancreas Tumor	Uni-ZAP XR	LP03
HTTA HTTB HTTC HTTD HTTE HTTF	Human Testes Tumor	Uni-ZAP XR	LP03
HAPA HAPB HAPC HAPM	Human Adult Pulmonary	Uni-ZAP XR	LP03
HETA HETB HETC HETD HETE HETF HETG HETH HETI	Human Endometrial Tumor	Uni-ZAP XR	LP03
HHFB HHFC HHFD HHFE HHFF HHFG HHFH HHFI	Human Fetal Heart	Uni-ZAP XR	LP03
HHPB HHPC HHPD HHPE HHPF HHPG HHPH	Human Hippocampus	Uni-ZAP XR	LP03
HCE1 HCE2 HCE3 HCE4 HCE5 HCEB HCEC HCED HCEE HCEF HCEG	Human Cerebellum	Uni-ZAP XR	LP03
HUVB HUVC HUVD HUVE	Human Umbilical Vein, Endo. remake	Uni-ZAP XR	LP03
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP03
HTAA HTAB HTAC HTAD HTAE	Human Activated T-Cells	Uni-ZAP XR	LP03
HFEA HFEB HFEC	Human Fetal Epithelium (Skin)	Uni-ZAP XR	LP03
HJPA HJPB HJPC HJPD	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Uni-ZAP XR	LP03
HESA	Human epithelioid sarcoma	Uni-Zap XR	LP03
HLTA HLTB HLTC HLTD HLTE HLTF	Human T-Cell Lymphoma	Uni-ZAP XR	LP03
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP03
HRDA HRDB HRDC HRDD HRDE HRDF	Human Rhabdomyosarcoma	Uni-ZAP XR	LP03
HCAA HCAB HCAC	Cem cells cyclohexamide treated	Uni-ZAP XR	LP03
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HSUA HSUB HSUC HSUM	Supt Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HT4A HT4C HT4D	Activated T-Cells, 12 hrs.	Uni-ZAP XR	LP03
HE9A HE9B HE9C HE9D HE9E HE9F HE9G HE9H HE9M HE9N	Nine Week Old Early Stage Human	Uni-ZAP XR	LP03
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP03
HT5A	Activated T-Cells, 24 hrs.	Uni-ZAP XR	LP03
HFGA HFGM	Human Fetal Brain	Uni-ZAP XR	LP03
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP03
HBGB HBGD	Human Primary Breast Cancer	Uni-ZAP XR	LP03
HBNA HBNB	Human Normal Breast	Uni-ZAP XR	LP03
HCAS	Cem Cells, cyclohexamide treated, subtra	Uni-ZAP XR	LP03
HHPS	Human Hippocampus, subtracted	pBS	LP03
HKCS HKCU	Human Colon Cancer, subtracted	pBS	LP03
HRGS	Raji cells, cyclohexamide treated, subtracted	pBS	LP03
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBS	LP03
HT4S	Activated T-Cells, 12 hrs, subtracted	Uni-ZAP XR	LP03
HCDA HCDB HCDC HCDD HCDE	Human Chondrosarcoma	Uni-ZAP XR	LP03
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP03
HTLA HTLB HTLC HTLD HTLE	Human adult testis, large inserts	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HTLF			
HLMA HLMC HLMD	Breast Lymph node cDNA library	Uni-ZAP XR	LP03
H6EA H6EB H6EC	HL-60, PMA 4H	Uni-ZAP XR	LP03
HTXA HTXB HTXC HTXD HTXE HTXF HTXG HTXH	Activated T-Cell (12hs)/Thiouridine labelledEco	Uni-ZAP XR	LP03
HNFA HNFB HNFC HNFD HNFE HNFF HNFG HNFH HNFJ	Human Neutrophil, Activated	Uni-ZAP XR	LP03
HTOB HTOC	HUMAN TONSILS, FRACTION 2	Uni-ZAP XR	LP03
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP03
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP03
HORB	Human OB HOS treated (10 nM E2) fraction I	Uni-ZAP XR	LP03
HSVA HSVB HSVC	Human Chronic Synovitis	Uni-ZAP XR	LP03
HROA	HUMAN STOMACH	Uni-ZAP XR	LP03
HBJA HBJB HBJC HBJD HBJE HBJF HBJG HBJH HBJI HBJJ HBJK	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP03
HCRA HCRB HCRC	human corpus colosum	Uni-ZAP XR	LP03
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP03
HDSA	Dermatofibrosarcoma Protuberance	Uni-ZAP XR	LP03
HMWA HMWB HMWC HMWD HMWE HMWF HMWG HMWH HMWI HMWJ	Bone Marrow Cell Line (RS4;11)	Uni-ZAP XR	LP03
HSOA	stomach cancer (human)	Uni-ZAP XR	LP03
HERA	SKIN	Uni-ZAP XR	LP03
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP03
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP03
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP03
HBCA HBCB	H. Lymph node breast Cancer	Uni-ZAP XR	LP03
HPWT	Human Prostate BPH, re-excision	Uni-ZAP XR	LP03
HFVG HFVH HFVI	Fetal Liver, subtraction II	pBS	LP03
HNFI	Human Neutrophils, Activated, re-excision	pBS	LP03
HBMB HBMC HBMD	Human Bone Marrow, re-excision	pBS	LP03
HKML HKMM HKMN	H. Kidney Medulla, re-excision	pBS	LP03
HKIX HKIY	H. Kidney Cortex, subtracted	pBS	LP03
HADT	H. Amygdala Depression, subtracted	pBS	LP03
H6AS	Hl-60, untreated, subtracted	Uni-ZAP XR	LP03
H6ES	HL-60, PMA 4H, subtracted	Uni-ZAP XR	LP03
H6BS	HL-60, RA 4h, Subtracted	Uni-ZAP XR	LP03
H6CS	HL-60, PMA 1d, subtracted	Uni-ZAP XR	LP03
HTXJ HTXK	Activated T-cell(12h)/Thiouridine-re-excision	Uni-ZAP XR	LP03
HMSA HMSB HMSC HMSD HMSE HMSF HMSG HMSH HMSI HMSJ HMSK	Monocyte activated	Uni-ZAP XR	LP03
HAGA HAGB HAGC HAGD HAGE HAGF	Human Amygdala	Uni-ZAP XR	LP03
HSRA HSRB HSRE	STROMAL -OSTEOCLASTOMA	Uni-ZAP XR	LP03
HSRD HSRF HSRG HSRH	Human Osteoclastoma Stromal Cells - unamplified	Uni-ZAP XR	LP03
HSQA HSQB HSQC HSQD HSQE	Stromal cell TF274	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HSQF HSQG			
HSKA HSKB HSKC HSKD HSKE HSKF HSKZ	Smooth muscle, serum treated	Uni-ZAP XR	LP03
HSLA HSLB HSLC HSLD HSLE HSLF HSLG	Smooth muscle,control	Uni-ZAP XR	LP03
HSDA HSDD HSDE HSDF HSDG HSDH	Spinal cord	Uni-ZAP XR	LP03
HPWS	Prostate-BPH subtracted II	pBS	LP03
HSKW HSKX HSKY	Smooth Muscle- HASTE normalized	pBS	LP03
HFPB HFPC HFPD	H. Frontal cortex,epileptic;re-excision	Uni-ZAP XR	LP03
HSDI HSDJ HSDK	Spinal Cord, re-excision	Uni-ZAP XR	LP03
HSKN HSKO	Smooth Muscle Serum Treated, Norm	pBS	LP03
HSKG HSKH HSKI	Smooth muscle, serum induced,re-exc	pBS	LP03
HFCA HFCB HFCC HFCD HFCE HFCF	Human Fetal Brain	Uni-ZAP XR	LP04
HPTA HPTB HPTD	Human Pituitary	Uni-ZAP XR	LP04
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP04
HE6B HE6C HE6D HE6E HE6F HE6G HE6S	Human Whole Six Week Old Embryo	Uni-ZAP XR	LP04
HSSA HSSB HSSC HSSD HSSE HSSF HSSG HSSH HSSI HSSJ HSSK	Human Synovial Sarcoma	Uni-ZAP XR	LP04
HE7T	7 Week Old Early Stage Human, subtracted	Uni-ZAP XR	LP04
HEPA HEPB HEPC	Human Epididymus	Uni-ZAP XR	LP04
HSNA HSNB HSNC HSNM HSNN	Human Synovium	Uni-ZAP XR	LP04
HPFB HPFC HPFD HPFE	Human Prostate Cancer, Stage C fraction	Uni-ZAP XR	LP04
HE2A HE2D HE2E HE2H HE2I HE2M HE2N HE2O	12 Week Old Early Stage Human	Uni-ZAP XR	LP04
HE2B HE2C HE2F HE2G HE2P HE2Q	12 Week Old Early Stage Human, II	Uni-ZAP XR	LP04
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP04
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP04
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP04
HWTA HWTB HWTC	wilm's tumor	Uni-ZAP XR	LP04
HBSD	Bone Cancer, re-excision	Uni-ZAP XR	LP04
HSGB	Salivary gland, re-excision	Uni-ZAP XR	LP04
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP04
HSXA HSXB HSXC HSXD	Human Substantia Nigra	Uni-ZAP XR	LP04
HSHA HSHB HSHC	Smooth muscle, IL1b induced	Uni-ZAP XR	LP04
HOUA HOUB HOUC HOUD HOUE	Adipocytes	Uni-ZAP XR	LP04
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP04
HELA HELB HELC HELD HELE HELF HELG HELH	Endothelial cells-control	Uni-ZAP XR	LP04
HEMA HEMB HEMC HEMD HEME HEMF HEMG HEMH	Endothelial-induced	Uni-ZAP XR	LP04
HBIA HBIB HBIC	Human Brain, Striatum	Uni-ZAP XR	LP04
HHSA HHSB HHSC HHSD HHSE	Human Hypothalmus,Schizophrenia	Uni-ZAP XR	LP04
HNGA HNGB HNGC HNGD HNGE HNGF HNGG HNGH HNGI HNGJ	neutrophils control	Uni-ZAP XR	LP04
HNHA HNHB HNHC HNHD HNHE HNHF HNHG HNHH HNHI HNHJ	Neutrophils IL-1 and LPS induced	Uni-ZAP XR	LP04
HSDB HSDC	STRIATUM DEPRESSION	Uni-ZAP XR	LP04

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HHPT	Hypothalamus	Uni-ZAP XR	LP04
HSAT HSAU HSAV HSAW HSAX HSAY HSAZ	Anergic T-cell	Uni-ZAP XR	LP04
HBMS HBMT HBMU HBMV HBMW HBMX	Bone marrow	Uni-ZAP XR	LP04
HOEA HOEB HOEC HOED HOEE HOEF HOEJ	Osteoblasts	Uni-ZAP XR	LP04
HAIA HAIB HAIC HAID HAIE HAIF	Epithelial-TNFa and INF induced	Uni-ZAP XR	LP04
HTGA HTGB HTGC HTGD	Apoptotic T-cell	Uni-ZAP XR	LP04
HMCA HMCB HMCC HMCD HMCE	Macrophage-oxLDL	Uni-ZAP XR	LP04
HMAA HMAB HMAC HMAD HMAE HMAF HMAG	Macrophage (GM-CSF treated)	Uni-ZAP XR	LP04
HPHA	Normal Prostate	Uni-ZAP XR	LP04
HPIA HPIB HPIC	LNCAP prostate cell line	Uni-ZAP XR	LP04
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP04
HOSE HOSF HOSG	Human Osteoclastoma, re-excision	Uni-ZAP XR	LP04
HTGE HTGF	Apoptotic T-cell, re-excision	Uni-ZAP XR	LP04
HMAJ HMAK	H Macrophage (GM-CSF treated), re-excision	Uni-ZAP XR	LP04
HACB HACC HACD	Human Adipose Tissue, re-excision	Uni-ZAP XR	LP04
HFPA	H. Frontal Cortex, Epileptic	Uni-ZAP XR	LP04
HFAA HFAB HFAC HFAD HFAE	Alzheimers, spongy change	Uni-ZAP XR	LP04
HFAM	Frontal Lobe, Dementia	Uni-ZAP XR	LP04
HMIA HMIB HMIC	Human Manic Depression Tissue	Uni-ZAP XR	LP04
HTSA HTSE HTSF HTSG HTSH	Human Thymus	pBS	LP05
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBS	LP05
HSAA HSAB HSAC	HSA 172 Cells	pBS	LP05
HSBA HSBB HSBC HSBM	HSC172 cells	pBS	LP05
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBS	LP05
HJBA HJBB HJBC HJBD	Jurkat T-Cell, S phase	pBS	LP05
HAFA HAFB	Aorta endothelial cells + TNF-a	pBS	LP05
HAWA HAWB HAWC	Human White Adipose	pBS	LP05
HTNA HTNB	Human Thyroid	pBS	LP05
HONA	Normal Ovary, Premenopausal	pBS	LP05
HARA HARB	Human Adult Retina	pBS	LP05
HLJA HLJB	Human Lung	pCMVSport 1	LP06
HOFM HOFN HOFO	H. Ovarian Tumor, II, OV5232	pCMVSport 2.0	LP07
HOGA HOGB HOGC	OV 10-3-95	pCMVSport 2.0	LP07
HCGL	CD34+cells, II	pCMVSport 2.0	LP07
HDLA	Hodgkin's Lymphoma I	pCMVSport 2.0	LP07
HDTA HDTB HDTC HDTD HDTE	Hodgkin's Lymphoma II	pCMVSport 2.0	LP07
HKAA HKAB HKAC HKAD HKAE HKAF HKAG HKAH	Keratinocyte	pCMVSport2.0	LP07
HCIM	CAPFINDER, Crohn's Disease, lib 2	pCMVSport 2.0	LP07
HKAL	Keratinocyte, lib 2	pCMVSport2.0	LP07
HKAT	Keratinocyte, lib 3	pCMVSport2.0	LP07
HNDA	Nasal polyps	pCMVSport2.0	LP07
HDRA	H. Primary Dendritic Cells,lib 3	pCMVSport2.0	LP07

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HOHA HOHB HOHC	Human Osteoblasts II	pCMVSport2.0	LP07
HLDA HLDB HLDC	Liver, Hepatoma	pCMVSport3.0	LP08
HLDN HLDO HLDP	Human Liver, normal	pCMVSport3.0	LP08
HMTA	pBMC stimulated w/ poly I/C	pCMVSport3.0	LP08
HNTA	NTERA2, control	pCMVSport3.0	LP08
HDPA HDPB HDPC HDPD HDPF HDPG HDPH HDPI HDPJ HDPK	Primary Dendritic Cells, lib 1	pCMVSport3.0	LP08
HDPM HDPN HDPO HDPP	Primary Dendritic cells,frac 2	pCMVSport3.0	LP08
HMUA HMUB HMUC	Myoloid Progenitor Cell Line	pCMVSport3.0	LP08
HHEA HHEB HHEC HHED	T Cell helper I	pCMVSport3.0	LP08
HHEM HHEN HHEO HHEP	T cell helper II	pCMVSport3.0	LP08
HEQA HEQB HEQC	Human endometrial stromal cells	pCMVSport3.0	LP08
HJMA HJMB	Human endometrial stromal cells-treated with progesterone	pCMVSport3.0	LP08
HSWA HSWB HSWC	Human endometrial stromal cells-treated with estradiol	pCMVSport3.0	LP08
HSYA HSYB HSYC	Human Thymus Stromal Cells	pCMVSport3.0	LP08
HLWA HLWB HLWC	Human Placenta	pCMVSport3.0	LP08
HRAA HRAB HRAC	Rejected Kidney, lib 4	pCMVSport3.0	LP08
HMTM	PCR, pBMC I/C treated	PCRII	LP09
HMJA	H. Meniingima, M6	pSport 1	LP10
HMKA HMKB HMKC HMKD HMKE	H. Meningima, M1	pSport 1	LP10
HUSG HUSI	Human umbilical vein endothelial cells, IL-4 induced	pSport 1	LP10
HUSX HUSY	Human Umbilical Vein Endothelial Cells, uninduced	pSport 1	LP10
HOFA	Ovarian Tumor I, OV5232	pSport 1	LP10
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport 1	LP10
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport 1	LP10
HADA HADC HADD HADE HADF HADG	Human Adipose	pSport 1	LP10
HOVA HOVB HOVC	Human Ovary	pSport 1	LP10
HTWB HTWC HTWD HTWE HTWF	Resting T-Cell Library,II	pSport 1	LP10
HMMA	Spleen metastic melanoma	pSport 1	LP10
HLYA HLYB HLYC HLYD HLYE	Spleen, Chronic lymphocytic leukemia	pSport 1	LP10
HCGA	CD34+ cell, I	pSport 1	LP10
HEOM HEON	Human Eosinophils	pSport 1	LP10
HTDA	Human Tonsil, Lib 3	pSport 1	LP10
HSPA	Salivary Gland, Lib 2	pSport 1	LP10
HCHA HCHB HCHC	Breast Cancer cell line, MDA 36	pSport 1	LP10
HCHM HCHN	Breast Cancer Cell line, angiogenic	pSport 1	LP10
HCIA	Crohn's Disease	pSport 1	LP10
HDAA HDAB HDAC	HEL cell line	pSport 1	LP10
HABA	Human Astrocyte	pSport 1	LP10
HUFA HUFB HUFC	Ulcerative Colitis	pSport 1	LP10
HNTM	NTERA2 + retinoic acid, 14 days	pSport 1	LP10
HDQA	Primary Dendritic cells,CapFinder2, frac 1	pSport 1	LP10
HDQM	Primary Dendritic Cells, CapFinder, frac	pSport 1	LP10

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	2		
HLDX	Human Liver, normal,CapFinder	pSport 1	LP10
HULA HULB HULC	Human Dermal Endothelial Cells,untreated	pSport1	LP10
HUMA	Human Dermal Endothelial cells,treated	pSport1	LP10
HCJA	Human Stromal Endometrial fibroblasts, untreated	pSport1	LP10
HCJM	Human Stromal endometrial fibroblasts, treated w/ estradiol	pSport1	LP10
HEDA	Human Stromal endometrial fibroblasts, treated with progesterone	pSport1	LP10
HFNA	Human ovary tumor cell OV350721	pSport1	LP10
HKGA HKGB HKGC HKGD	Merkel Cells	pSport1	LP10
HISA HISB HISC	Pancreas Islet Cell Tumor	pSport1	LP10
HLSA	Skin, burned	pSport1	LP10
HBZA	Prostate,BPH, Lib 2	pSport 1	LP10
HBZS	Prostate BPH,Lib 2, subtracted	pSport 1	LP10
HFIA HFIB HFIC	Synovial Fibroblasts (control)	pSport 1	LP10
HFIH HFII HFIJ	Synovial hypoxia	pSport 1	LP10
HFIT HFIU HFIV	Synovial IL-1/TNF stimulated	pSport 1	LP10
HGCA	Messangial cell, frac 1	pSport1	LP10
HMVA HMVB HMVC	Bone Marrow Stromal Cell, untreated	pSport1	LP10
HFIX HFIY HFIZ	Synovial Fibroblasts (Il1/TNF), subt	pSport1	LP10
HFOX HFOY HFOZ	Synovial hypoxia-RSF subtracted	pSport1	LP10
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP11
HLIA HLIB HLIC	Human Liver	pCMVSport 1	LP012
HHBA HHBB HHBC HHBD HHBE	Human Heart	pCMVSport 1	LP012
HBBA HBBB	Human Brain	pCMVSport 1	LP012
HLJA HLJB HLJC HLJD HLJE	Human Lung	pCMVSport 1	LP012
HOGA HOGB HOGC	Ovarian Tumor	pCMVSport 2.0	LP012
HTJM	Human Tonsils, Lib 2	pCMVSport 2.0	LP012
HAMF HAMG	KMH2	pCMVSport 3.0	LP012
HAJA HAJB HAJC	L428	pCMVSport 3.0	LP012
HWBA HWBB HWBC HWBD HWBE	Dendritic cells, pooled	pCMVSport 3.0	LP012
HWAA HWAB HWAC HWAD HWAE	Human Bone Marrow, treated	pCMVSport 3.0	LP012
HYAA HYAB HYAC	B Cell lymphoma	pCMVSport 3.0	LP012
HWHG HWHH HWHI	Healing groin wound, 6.5 hours post incision	pCMVSport 3.0	LP012
HWHP HWHQ HWHR	Healing groin wound; 7.5 hours post incision	pCMVSport 3.0	LP012
HARM	Healing groin wound - zero hr post-incision (control)	pCMVSport 3.0	LP012
HBIM	Olfactory epithelium; nasalcavity	pCMVSport 3.0	LP012
HWDA	Healing Abdomen wound; 70&90 min post incision	pCMVSport 3.0	LP012
HWEA	Healing Abdomen Wound;15 days post incision	pCMVSport 3.0	LP012
HWJA	Healing Abdomen Wound;21&29 days	pCMVSport 3.0	LP012
HNAL	Human Tongue, frac 2	pSport1	LP012
HMJA	H. Meniingima, M6	pSport1	LP012
HMKA HMKB HMKC HMKD HMKE	H. Meningima, M1	pSport1	LP012

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HOFA	Ovarian Tumor I, OV5232	pSport1	LP012
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport1	LP012
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport1	LP012
HMMA HMMB HMMC	Spleen metastic melanoma	pSport1	LP012
HTDA	Human Tonsil, Lib 3	pSport1	LP012
HDBA	Human Fetal Thymus	pSport1	LP012
HDUA	Pericardium	pSport1	LP012
HBZA	Prostate,BPH, Lib 2	pSport1	LP012
HWCA	Larynx tumor	pSport1	LP012
HWKA	Normal lung	pSport1	LP012
HSMB	Bone marrow stroma,treated	pSport1	LP012
HBHM	Normal trachea	pSport1	LP012
HLFC	Human Larynx	pSport1	LP012
HLRB	Siebben Polyposis	pSport1	LP012
HNIA	Mammary Gland	pSport1	LP012
HNJB	Palate carcinoma	pSport1	LP012
HNKA	Palate normal	pSport1	LP012
HMZA	Pharynx carcinoma	pSport1	LP012
HABG	Cheek Carcinoma	pSport1	LP012
HMZM	Pharynx Carcinoma	pSport1	LP012
HDRM	Larynx Carcinoma	pSport1	LP012
HVAA	Pancreas normal PCA4 No	pSport1	LP012
HICA	Tongue carcinoma	pSport1	LP012
HUKA HUKB HUKC HUKD HUKE	Human Uterine Cancer	Lambda ZAP II	LP013
HFFA	Human Fetal Brain, random primed	Lambda ZAP II	LP013
HTUA	Activated T-cell labeled with 4-thioluri	Lambda ZAP II	LP013
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP013
HMEB	Human microvascular Endothelial cells, fract. B	Lambda ZAP II	LP013
HUSH	Human Umbilical Vein Endothelial cells, fract. A, re-excision	Lambda ZAP II	LP013
HLQC HLQD	Hepatocellular tumor, re-excision	Lambda ZAP II	LP013
HTWJ HTWK HTWL	Resting T-cell, re-excision	Lambda ZAP II	LP013
HF6S	Human Whole 6 week Old Embryo (II), subt	pBluescript	LP013
HHPS	Human Hippocampus, subtracted	pBluescript	LP013
HL1S	LNCAP, differential expression	pBluescript	LP013
HLHS HLHT	Early Stage Human Lung, Subtracted	pBluescript	LP013
HSUS	Supt cells, cyclohexamide treated, subtracted	pBluescript	LP013
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBluescript	LP013
HSDS	H. Striatum Depression, subtracted	pBluescript	LP013
HPTZ	Human Pituitary, Subtracted VII	pBluescript	LP013
HSDX	H. Striatum Depression, subt II	pBluescript	LP013
HSDZ	H. Striatum Depression, subt	pBluescript	LP013
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBluescript SK-	LP013
HRTA	Colorectal Tumor	pBluescript SK-	LP013
HSBA HSBB HSBC HSBM	HSC172 cells	pBluescript SK-	LP013
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBluescript SK-	LP013
HJBA HJBB HJBC HJBD	Jurkat T-cell, S1 phase	pBluescript SK-	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HTNA HTNB	Human Thyroid	pBluescript SK-	LP013
HAHA HAHB	Human Adult Heart	Uni-ZAP XR	LP013
HE6A	Whole 6 week Old Embryo	Uni-ZAP XR	LP013
HFCA HFCB HFCC HFCD HFCE	Human Fetal Brain	Uni-ZAP XR	LP013
HFKC HFKD HFKE HFKF HFKG	Human Fetal Kidney	Uni-ZAP XR	LP013
HGBA HGBD HGBE HGBF HGBG	Human Gall Bladder	Uni-ZAP XR	LP013
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP013
HTEA HTEB HTEC HTED HTEE	Human Testes	Uni-ZAP XR	LP013
HTTA HTTB HTTC HTTD HTTE	Human Testes Tumor	Uni-ZAP XR	LP013
HYBA HYBB	Human Fetal Bone	Uni-ZAP XR	LP013
HFLA	Human Fetal Liver	Uni-ZAP XR	LP013
HHFB HHFC HHFD HHFE HHFF	Human Fetal Heart	Uni-ZAP XR	LP013
HUVB HUVC HUVD HUVE	Human Umbilical Vein, End. remake	Uni-ZAP XR	LP013
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP013
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP013
HTAA HTAB HTAC HTAD HTAE	Human Activated T-cells	Uni-ZAP XR	LP013
HFEA HFEB HFEC	Human Fetal Epithelium (skin)	Uni-ZAP XR	LP013
HJPA HJPB HJPC HJPD	Human Jurkat Membrane Bound Polysomes	Uni-ZAP XR	LP013
HESA	Human Epithelioid Sarcoma	Uni-ZAP XR	LP013
HALS	Human Adult Liver, Subtracted	Uni-ZAP XR	LP013
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP013
HCAA HCAB HCAC	Cem cells, cyclohexamide treated	Uni-ZAP XR	LP013
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP013
HE9A HE9B HE9C HE9D HE9E	Nine Week Old Early Stage Human	Uni-ZAP XR	LP013
HSFA	Human Fibrosarcoma	Uni-ZAP XR	LP013
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP013
HTRA	Human Trachea Tumor	Uni-ZAP XR	LP013
HE2A HE2D HE2E HE2H HE2I	12 Week Old Early Stage Human	Uni-ZAP XR	LP013
HE2B HE2C HE2F HE2G HE2P	12 Week Old Early Stage Human, II	Uni-ZAP XR	LP013
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP013
HBGA	Human Primary Breast Cancer	Uni-ZAP XR	LP013
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP013
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP013
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP013
HTOA HTOD HTOE HTOF HTOG	human tonsils	Uni-ZAP XR	LP013
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP013
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP013
HOQB	Human OB HOS treated (1 nM E2) fraction I	Uni-ZAP XR	LP013
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP013
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP013
HROA HROC	HUMAN STOMACH	Uni-ZAP XR	LP013
HBJA HBJB HBJC HBJD HBJE	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP013
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP013
HCPA	Corpus Callosum	Uni-ZAP XR	LP013
HSOA	stomach cancer (human)	Uni-ZAP XR	LP013
HERA	SKIN	Uni-ZAP XR	LP013
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP013
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HWTA HWTB HWTC	wilm's tumor	Uni-ZAP XR	LP013
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP013
HAPN HAPO HAPP HAPQ HAPR	Human Adult Pulmonary;re-excision	Uni-ZAP XR	LP013
HLTG HLTH	Human T-cell lymphoma;re-excision	Uni-ZAP XR	LP013
HAHC HAHD HAHE	Human Adult Heart;re-excision	Uni-ZAP XR	LP013
HAGA HAGB HAGC HAGD HAGE	Human Amygdala	Uni-ZAP XR	LP013
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP013
HSHA HSHB HSHC	Smooth muscle, IL1b induced	Uni-ZAP XR	LP013
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP013
HPIA HPIB HPIC	LNCAP prostate cell line	Uni-ZAP XR	LP013
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP013
HBTA	Bone Marrow Stroma. TNF&LPS ind	Uni-ZAP XR	LP013
HMCF HMCG HMCH HMCI HMCJ	Macrophage-oxLDL; re-excision	Uni-ZAP XR	LP013
HAGG HAGH HAGI	Human Amygdala;re-excision	Uni-ZAP XR	LP013
HACA	H. Adipose Tissue	Uni-ZAP XR	LP013
HKFB	K562 + PMA (36 hrs).re-excision	ZAP Express	LP013
HCWT HCWU HCWV	CD34 positive cells (cord blood),re-ex	ZAP Express	LP013
HBWA	Whole brain	ZAP Express	LP013
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP013
HAVM	Temporal cortex-Alzheizmer	pT-Adv	LP014
HAVT	Hippocampus, Alzheimer Subtracted	pT-Adv	LP014
HHAS	CHME Cell Line	Uni-ZAP XR	LP014
HAJR	Larynx normal	pSport 1	LP014
HWLE HWLF HWLG HWLH	Colon Normal	pSport 1	LP014
HCRM HCRN HCRO	Colon Carcinoma	pSport 1	LP014
HWLI HWLJ HWLK	Colon Normal	pSport 1	LP014
HWLQ HWLR HWLS HWLT	Colon Tumor	pSport 1	LP014
HBFM	Gastrocnemius Muscle	pSport 1	LP014
HBOD HBOE	Quadriceps Muscle	pSport 1	LP014
HBKD HBKE	Soleus Muscle	pSport 1	LP014
HCCM	Pancreatic Langerhans	pSport 1	LP014
HWGA	Larynx carcinoma	pSport 1	LP014
HWGM HWGN	Larynx carcinoma	pSport 1	LP014
HWLA HWLB HWLC	Normal colon	pSport 1	LP014
HWLM HWLN	Colon Tumor	pSport 1	LP014
HVAM HVAN HVAO	Pancreas Tumor	pSport 1	LP014
HWGQ	Larynx carcinoma	pSport 1	LP014
HAQM HAQN	Salivary Gland	pSport 1	LP014
HASM	Stomach; normal	pSport 1	LP014
HBCM	Uterus; normal	pSport 1	LP014
HCDM	Testis; normal	pSport 1	LP014
HDJM	Brain; normal	pSport 1	LP014
HEFM	Adrenal Gland,normal	pSport 1	LP014
HBAA	Rectum normal	pSport 1	LP014
HFDM	Rectum tumour	pSport 1	LP014
HGAM	Colon, normal	pSport 1	LP014
HHMM	Colon, tumour	pSport 1	LP014
HCLB HCLC	Human Lung Cancer	Lambda Zap II	LP015
HRLA	L1 Cell line	ZAP Express	LP015

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HHAM	Hypothalamus. Alzheimer's	pCMVSport 3.0	LP015
HKBA	Ku 812F Basophils Line	pSport 1	LP015
HS2S	Saos2. Dexamethosome Treated	pSport 1	LP016
HA5A	Lung Carcinoma A549 TNFalpha activated	pSport 1	LP016
HTFM	TF-1 Cell Line GM-CSF Treated	pSport 1	LP016
HYAS	Thyroid Tumour	pSport 1	LP016
HUTS	Larynx Normal	pSport 1	LP016
HXOA	Larynx Tumor	pSport 1	LP016
HEAH	Ea.hy.926 cell line	pSport 1	LP016
HINA	Adenocarcinoma Human	pSport 1	LP016
HRMA	Lung Mesothelium	pSport 1	LP016
HLCL	Human Pre-Differentiated Adipocytes	Uni-Zap XR	LP017
HS2A	Saos2 Cells	pSport 1	LP020
HS2I	Saos2 Cells; Vitamin D3 Treated	pSport 1	LP020
HUCM	CHME Cell Line, untreated	pSport 1	LP020
HEPN	Aryepiglottis Normal	pSport 1	LP020
HPSN	Sinus Piniformis Tumour	pSport 1	LP020
HNSA	Stomach Normal	pSport 1	LP020
HNSM	Stomach Tumour	pSport 1	LP020
HNLA	Liver Normal Met5No	pSport 1	LP020
HUTA	Liver Tumour Met 5 Tu	pSport 1	LP020
HOCN	Colon Normal	pSport 1	LP020
HOCT	Colon Tumor	pSport 1	LP020
HTNT	Tongue Tumour	pSport 1	LP020
HLXN	Larynx Normal	pSport 1	LP020
HLXT	Larynx Tumour	pSport 1	LP020
HTYN	Thymus	pSport 1	LP020
HPLN	Placenta	pSport 1	LP020
HTNG	Tongue Normal	pSport 1	LP020
HZAA	Thyroid Normal (SDCA2 No)	pSport 1	LP020
HWES	Thyroid Thyroiditis	pSport 1	LP020
HFHD	Ficolled Human Stromal Cells, 5Fu treated	pTrip1Ex2	LP021
HFHM,HFHN	Ficolled Human Stromal Cells, Untreated	pTrip1Ex2	LP021
HPCI	Hep G2 Cells, lambda library	lambda Zap-CMV XR	LP021
HBCA,HBCB,HBCC	H. Lymph node breast Cancer	Uni-ZAP XR	LP021
HCOK	Chondrocytes	pSPORT1	LP022
HDCA. HDCB, HDCC	Dendritic Cells From CD34 Cells	pSPORT1	LP022
HDMA, HDMB	CD40 activated monocyte dendritic cells	pSPORT1	LP022
HDDM. HDDN, HDDO	LPS activated derived dendritic cells	pSPORT1	LP022
HPCR	Hep G2 Cells, PCR library	lambda Zap-CMV XR	LP022
HAAA, HAAB, HAAC	Lung, Cancer (4005313A3): Invasive Poorly Differentiated Lung Adenocarcinoma	pSPORT1	LP022
HIPA. HIPB, HIPC	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	pSPORT1	LP022
HOOH. HOOI	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low	pSPORT1	LP022

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	Malignant Pot		
HIDA	Lung, Normal: (4005313 B1)	pSPORT1	LP022
HUJA.HUJB.HUJC.HUJD.HUJE	B-Cells	pCMVSport 3.0	LP022
HNOA.HNOB.HNOC,HNOD	Ovary, Normal: (9805C040R)	pSPORT1	LP022
HNLM	Lung, Normal: (4005313 B1)	pSPORT1	LP022
HSCL	Stromal Cells	pSPORT1	LP022
HAAX	Lung, Cancer: (4005313 A3) Invasive Poorly-differentiated Metastatic lung adenocarcinoma	pSPORT1	LP022
HUUA.HUUB.HUUC.HUUD	B-cells (unstimulated)	pTrip1Ex2	LP022
HWWA.HWWB.HWWC.HWWD,HWWE.HWWF.HWWG	B-cells (stimulated)	pSPORT1	LP022
HCCC	Colon, Cancer: (9808C064R)	pCMVSport 3.0	LP023
HPDO HPDP HPDQ HPDR HPD	Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma	pSport 1	LP023
HPCO HPCP HPCQ HPCT	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	pSport 1	LP023
HOCM HOCO HOCP HOCQ	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	pSport 1	LP023
HCBM HCBN HCBO	Breast, Cancer: (4004943 A5)	pSport 1	LP023
HNBT HNBU HNBV	Breast, Normal: (4005522B2)	pSport 1	LP023
HBCP HBCQ	Breast, Cancer: (4005522 A2)	pSport 1	LP023
HBCJ	Breast, Cancer: (9806C012R)	pSport 1	LP023
HSAM HSAN	Stromal cells 3.88	pSport 1	LP023
HVCA HVCB HVCC HVCD	Ovary, Cancer: (4004332 A2)	pSport 1	LP023
HSCK HSEN HSEO	Stromal cells (HBM3.18)	pSport 1	LP023
HSCP HSCQ	stromal cell clone 2.5	pSport 1	LP023
HUXA	Breast Cancer: (4005385 A2)	pSport 1	LP023
HCOM HCON HCOO HCOP HCOQ	Ovary, Cancer (4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	pSport 1	LP023
HBNM	Breast, Cancer: (9802C020E)	pSport 1	LP023
HVVA HVVB HVVC HVVD HVVE	Human Bone Marrow, treated	pSport 1	LP023

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 5. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to the nucleotide sequence of SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ^{32}P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982).) The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the nucleotide sequence of SEQ ID NO:X are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 μl of reaction mixture with 0.5 ug of the above cDNA template. A convenient reaction mixture is 1.5-5 mM $MgCl_2$, 0.01% (w/v) gelatin, 20 μM each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not

limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., Nucleic Acids Res. 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the sequence corresponding to SEQ ID NO:X, according to the method described in Example 1. (See also, Sambrook.)

Example 3: Tissue specific expression analysis

The Human Genome Sciences, Inc. (HGS) database is derived from sequencing tissue specific cDNA libraries. Libraries generated from a particular tissue are selected and the specific tissue expression pattern of EST groups or assembled contigs within these libraries is determined by comparison of the expression patterns of those groups or contigs within the entire database. ESTs which show tissue specific expression are selected.

The original clone from which the specific EST sequence was generated, is obtained from the catalogued library of clones and the insert amplified by PCR using methods known in the art. The PCR product is denatured then transferred in 96 well format to a nylon membrane (Schleicher and Scheull) generating an array filter of tissue specific clones. Housekeeping genes, maize genes, and known tissue specific genes are included on the filters. These targets can be used in signal normalization and to validate assay sensitivity. Additional targets are included to monitor probe length and specificity of hybridization.

Radioactively labeled hybridization probes are generated by first strand cDNA synthesis per the manufacturer's instructions (Life Technologies) from mRNA/RNA samples prepared from the specific tissue being analyzed. The hybridization probes are purified by gel exclusion chromatography, quantitated, and hybridized with the array filters in hybridization bottles at 65°C overnight. The filters are washed under stringent conditions and signals are captured using a Fuji phosphorimager.

Data is extracted using AIS software and following background subtraction, signal normalization is performed. This includes a normalization of filter-wide expression levels between different experimental runs. Genes that are differentially expressed in the tissue of interest are identified and the full length sequence of these clones is generated.

Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute

cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

Example 5: Bacterial Expression of a Polypeptide

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 ($O.D.^{600}$) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM immidazole. Immidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4° C or frozen at -80° C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction

sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

Example 6: Purification of a Polypeptide from an Inclusion Body

The following alternative method can be used to purify a polypeptide expressed in *E coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfuidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 μm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A_{280} monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 μg of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under

control of a weak Drosophila promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., Virology 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon, is amplified using the PCR protocol described in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("Geneclean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

Five µg of a plasmid containing the polynucleotide is co-transfected with 1.0 µg of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA",

Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One µg of BaculoGold™ virus DNA and 5 µg of the plasmid are mixed in a sterile well of a microtiter plate containing 50 µl of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 µl Lipofectin plus 90 µl Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 µCi of ^{35}S-methionine and 5 µCi ^{35}S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

Example 8: Expression of a Polypeptide in Mammalian Cells

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLVI, HIVI and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSport 2.0, and pCMVSport 3.0. Mammalian host cells that could be used include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as DHFR, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used

for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No.209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the vector does not need a second signal peptide. Alternatively, if a naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five µg of the expression plasmid pC6 or pC4 is cotransfected with 0.5 µg of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10,

25, or 50 ng/ml of metothrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 μM, 2 μM, 5 μM, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200 μM. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

Example 9: Protein Fusions

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the halflife time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the

vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the polypeptide of the present invention, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:
GGGATCCGGAGCCCAAATCTTCTGACAAAACTCACACATGCCCACCGTGCCCAG
CACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGA
CACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGGTGGACGTAAGC
CACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAT
AATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC
AGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGC
AAGGTCTCCAACAAAGCCCTCCCAACCCCCATCGAGAAAACCATCTCCAAAGCC
AAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAG
CTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAAGC
GACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGAC
CACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACC
GTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCAT
GAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAAT
GAGTGCGACGGCCGCGACTCTAGAGGAT (SEQ ID NO:837)

Example 10: Production of an Antibody from a Polypeptide

a) Hybridoma Technology

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) As one example of such methods, cells expressing polypeptide of the present invention are administered to an animal to induce the production of sera containing polyclonal antibodies. In a preferred method, a preparation of polypeptide

of the present invention is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

Monoclonal antibodies specific for polypeptide of the present invention are prepared using hybridoma technology. (Kohler et al., Nature 256:495 (1975); Kohler et al., Eur. J. Immunol. 6:511 (1976); Kohler et al., Eur. J. Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell Hybridomas, Elsevier, N.Y., pp. 563-681 (1981)). In general, an animal (preferably a mouse) is immunized with polypeptide of the present invention or, more preferably, with a secreted polypeptide of the present invention-expressing cell. Such polypeptide-expressing cells are cultured in any suitable tissue culture medium, preferably in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 μg/ml of streptomycin.

The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (Gastroenterology 80:225-232 (1981)). The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide of the present invention.

Alternatively, additional antibodies capable of binding to polypeptide of the present invention can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the polypeptide of the present invention-specific antibody can be blocked by polypeptide of the present invention. Such antibodies comprise anti-idiotypic antibodies to the polypeptide of the present invention-specific antibody and are used to immunize an animal to induce formation of further polypeptide of the present invention-specific antibodies.

For in vivo use of antibodies in humans, an antibody is "humanized". Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric and humanized antibodies are known in the art and are discussed herein. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

b) Isolation Of Antibody Fragments Directed Against Polypeptide of the Present Invention From A Library Of scFvs

Naturally occurring V-genes isolated from human PBLs are constructed into a library of antibody fragments which contain reactivities against polypeptide of the present invention to which the donor may or may not have been exposed (see e.g., U.S. Patent 5,885,793 incorporated herein by reference in its entirety).

Rescue of the Library. A library of scFvs is constructed from the RNA of human PBLs as described in PCT publication WO 92/01047. To rescue phage displaying antibody fragments, approximately 109 E. coli harboring the phagemid are used to inoculate 50 ml of 2xTY containing 1% glucose and 100 µg/ml of ampicillin (2xTY-AMP-GLU) and grown to an O.D. of 0.8 with shaking. Five ml of this culture is used to innoculate 50 ml of 2xTY-AMP-GLU, 2 x 108 TU of delta gene 3 helper (M13 delta gene III, see PCT publication WO 92/01047) are added and the culture incubated at 37°C for 45 minutes without shaking and then at 37°C for 45 minutes with shaking. The culture is centrifuged at 4000 r.p.m. for 10 min. and the pellet resuspended in 2 liters of 2xTY containing 100 µg/ml ampicillin and 50 ug/ml kanamycin and grown overnight. Phage are prepared as described in PCT publication WO 92/01047.

M13 delta gene III is prepared as follows: M13 delta gene III helper phage does not encode gene III protein, hence the phage(mid) displaying antibody fragments have a greater avidity of binding to antigen. Infectious M13 delta gene III particles are made by growing the helper phage in cells harboring a pUC19 derivative supplying the wild type gene III protein during phage morphogenesis. The culture is incubated for 1 hour at 37° C without shaking and then for a further hour at 37°C with shaking. Cells are spun down (IEC-Centra

8,400 r.p.m. for 10 min), resuspended in 300 ml 2xTY broth containing 100 μg ampicillin/ml and 25 μg kanamycin/ml (2xTY-AMP-KAN) and grown overnight, shaking at 37°C. Phage particles are purified and concentrated from the culture medium by two PEG-precipitations (Sambrook et al., 1990), resuspended in 2 ml PBS and passed through a 0.45 μm filter (Minisart NML; Sartorius) to give a final concentration of approximately 1013 transducing units/ml (ampicillin-resistant clones).

Panning of the Library. Immunotubes (Nunc) are coated overnight in PBS with 4 ml of either 100 μg/ml or 10 μg/ml of a polypeptide of the present invention. Tubes are blocked with 2% Marvel-PBS for 2 hours at 37°C and then washed 3 times in PBS. Approximately 1013 TU of phage is applied to the tube and incubated for 30 minutes at room temperature tumbling on an over and under turntable and then left to stand for another 1.5 hours. Tubes are washed 10 times with PBS 0.1% Tween-20 and 10 times with PBS. Phage are eluted by adding 1 ml of 100 mM triethylamine and rotating 15 minutes on an under and over turntable after which the solution is immediately neutralized with 0.5 ml of 1.0M Tris-HCl, pH 7.4. Phage are then used to infect 10 ml of mid-log E. coli TG1 by incubating eluted phage with bacteria for 30 minutes at 37°C. The E. coli are then plated on TYE plates containing 1% glucose and 100 μg/ml ampicillin. The resulting bacterial library is then rescued with delta gene 3 helper phage as described above to prepare phage for a subsequent round of selection. This process is then repeated for a total of 4 rounds of affinity purification with tube-washing increased to 20 times with PBS, 0.1% Tween-20 and 20 times with PBS for rounds 3 and 4.

Characterization of Binders. Eluted phage from the 3rd and 4th rounds of selection are used to infect E. coli HB 2151 and soluble scFv is produced (Marks, et al., 1991) from single colonies for assay. ELISAs are performed with microtitre plates coated with either 10 pg/ml of the polypeptide of the present invention in 50 mM bicarbonate pH 9.6. Clones positive in ELISA are further characterized by PCR fingerprinting (see, e.g., PCT publication WO 92/01047) and then by sequencing. These ELISA positive clones may also be further characterized by techniques known in the art, such as, for example, epitope mapping, binding affinity, receptor signal transduction, ability to block or competitively inhibit antibody/antigen binding, and competitive agonistic or antagonistic activity.

Example 11: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X; and/or the nucleotide sequence of the related cDNA in the cDNA clone contained in a deposited library. Suggested PCR conditions consist of 35 cycles at 95 degrees C for 30 seconds; 60-120 seconds at 52-58 degrees C; and 60-120 seconds at 70 degrees C, using buffer solutions described in Sidransky et al., Science 252:706 (1991).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton et al., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-triphosphate (Boehringer Manheim), and FISH performed as described in Johnson et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image

collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 12: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 13: Formulation

The invention also provides methods of treatment and/or prevention of diseases or disorders (such as, for example, any one or more of the diseases or disorders disclosed herein) by administration to a subject of an effective amount of a Therapeutic. By therapeutic is meant a polynucleotides or polypeptides of the invention (including fragments and variants), agonists or antagonists thereof, and/or antibodies thereto, in combination with a pharmaceutically acceptable carrier type (e.g., a sterile carrier).

The Therapeutic will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the Therapeutic alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of the Therapeutic administered parenterally per dose will be in the range of about 1ug/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the Therapeutic is typically administered at a dose rate of about 1 ug/kg/hour to about 50 ug/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Therapeutics can be are administered orally, rectally, parenterally, intracistemally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics are administered orally, rectally, parenterally, intracistemally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics include suitable polymeric materials (such as, for example, semi-permeable polymer matrices in the form of shaped articles, e.g., films, or mirocapsules), suitable hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, and sparingly soluble derivatives (such as, for example, a sparingly soluble salt).

Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman et al., Biopolymers 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (Langer et al., J. Biomed. Mater. Res. 15:167-277 (1981), and Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (Langer et al., Id.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988).

Sustained-release Therapeutics also include liposomally entrapped Therapeutics of the invention (*see* generally, Langer, *Science* 249:1527-1533 (1990); Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 317 -327 and 353-365 (1989)). Liposomes containing the Therapeutic are prepared by methods known per se: DE 3,218,121; Epstein et al., Proc. Natl. Acad. Sci. (USA) 82:3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci.(USA) 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal Therapeutic.

In yet an additional embodiment, the Therapeutics of the invention are delivered by way of a pump (*see* Langer, *supra*; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987);

Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)).

Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

For parenteral administration, in one embodiment, the Therapeutic is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to the Therapeutic.

Generally, the formulations are prepared by contacting the Therapeutic uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The Therapeutic is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any pharmaceutical used for therapeutic administration can be sterile. Sterility is

readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutics generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Therapeutics ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous Therapeutic solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized Therapeutic using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the Therapeutics of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the Therapeutics may be employed in conjunction with other therapeutic compounds.

The Therapeutics of the invention may be administered alone or in combination with adjuvants. Adjuvants that may be administered with the Therapeutics of the invention include, but are not limited to, alum, alum plus deoxycholate (ImmunoAg), MTP-PE (Biocine Corp.), QS21 (Genentech, Inc.), BCG, and MPL. In a specific embodiment, Therapeutics of the invention are administered in combination with alum. In another specific embodiment, Therapeutics of the invention are administered in combination with QS-21. Further adjuvants that may be administered with the Therapeutics of the invention include, but are not limited to, Monophosphoryl lipid immunomodulator, AdjuVax 100a, QS-21, QS-18, CRL1005, Aluminum salts, MF-59, and Virosomal adjuvant technology. Vaccines that may be administered with the Therapeutics of the invention include, but are not limited to, vaccines directed toward protection against MMR (measles, mumps, rubella), polio, varicella, tetanus/diptheria, hepatitis A, hepatitis B, haemophilus influenzae B, whooping cough, pneumonia, influenza, Lyme's Disease, rotavirus, cholera, yellow fever, Japanese encephalitis, poliomyelitis, rabies, typhoid fever, and pertussis. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or

concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

The Therapeutics of the invention may be administered alone or in combination with other therapeutic agents. Therapeutic agents that may be administered in combination with the Therapeutics of the invention, include but not limited to, other members of the TNF family, chemotherapeutic agents, antibiotics, steroidal and non-steroidal anti-inflammatories, conventional immunotherapeutic agents, cytokines and/or growth factors. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

In one embodiment, the Therapeutics of the invention are administered in combination with members of the TNF family. TNF, TNF-related or TNF-like molecules that may be administered with the Therapeutics of the invention include, but are not limited to, soluble forms of TNF-alpha, lymphotoxin-alpha (LT-alpha, also known as TNF-beta), LT-beta (found in complex heterotrimer LT-alpha2-beta), OPGL, FasL, CD27L, CD30L, CD40L, 4-1BBL, DcR3, OX40L, TNF-gamma (International Publication No. WO 96/14328), AIM-I (International Publication No. WO 97/33899), endokine-alpha (International Publication No. WO 98/07880), TR6 (International Publication No. WO 98/30694), OPG, and neutrokine-alpha (International Publication No. WO 98/18921, OX40, and nerve growth factor (NGF), and soluble forms of Fas, CD30, CD27, CD40 and 4-IBB, TR2 (International Publication No. WO 96/34095), DR3 (International Publication No. WO 97/33904), DR4 (International Publication No. WO 98/32856), TR5 (International Publication No. WO 98/30693), TR6 (International Publication No. WO 98/30694), TR7 (International Publication No. WO 98/41629), TRANK, TR9 (International Publication No. WO 98/56892),TR10 (International Publication No. WO 98/54202), 312C2 (International Publication No. WO 98/06842), and TR12, and soluble forms CD154, CD70, and CD153.

In certain embodiments, Therapeutics of the invention are administered in combination with antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors. Nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, RETROVIR™ (zidovudine/AZT), VIDEX™ (didanosine/ddI), HIVID™ (zalcitabine/ddC), ZERIT™ (stavudine/d4T), EPIVIR™ (lamivudine/3TC), and COMBIVIR™ (zidovudine/lamivudine). Non-nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, VIRAMUNE™ (nevirapine), RESCRIPTOR™ (delavirdine), and SUSTIVA™ (efavirenz). Protease inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, CRIXIVAN™ (indinavir), NORVIR™ (ritonavir), INVIRASE™ (saquinavir), and VIRACEPT™ (nelfinavir). In a specific embodiment, antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors may be used in any combination with Therapeutics of the invention to treat AIDS and/or to prevent or treat HIV infection.

In other embodiments, Therapeutics of the invention may be administered in combination with anti-opportunistic infection agents. Anti-opportunistic agents that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, ATOVAQUONE™, ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, ETHAMBUTOL™, RIFABUTIN™, CLARITHROMYCIN™, AZITHROMYCIN™, GANCICLOVIR™, FOSCARNET™, CIDOFOVIR™, FLUCONAZOLE™, ITRACONAZOLE™, KETOCONAZOLE™, ACYCLOVIR™, FAMCICOLVIR™, PYRIMETHAMINE™, LEUCOVORIN™, NEUPOGEN™ (filgrastim/G-CSF), and LEUKINE™ (sargramostim/GM-CSF). In a specific embodiment, Therapeutics of the invention are used in any combination with TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, and/or ATOVAQUONE™ to prophylactically treat or prevent an opportunistic *Pneumocystis carinii* pneumonia infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, and/or ETHAMBUTOL™ to prophylactically treat or

prevent an opportunistic *Mycobacterium avium* complex infection. In another specific embodiment, Therapeutics of the invention are used in any combination with RIFABUTIN™, CLARITHROMYCIN™, and/or AZITHROMYCIN™ to prophylactically treat or prevent an opportunistic *Mycobacterium tuberculosis* infection. In another specific embodiment, Therapeutics of the invention are used in any combination with GANCICLOVIR™, FOSCARNET™, and/or CIDOFOVIR™ to prophylactically treat or prevent an opportunistic cytomegalovirus infection. In another specific embodiment, Therapeutics of the invention are used in any combination with FLUCONAZOLE™, ITRACONAZOLE™, and/or KETOCONAZOLE™ to prophylactically treat or prevent an opportunistic fungal infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ACYCLOVIR™ and/or FAMCICOLVIR™ to prophylactically treat or prevent an opportunistic herpes simplex virus type I and/or type II infection. In another specific embodiment, Therapeutics of the invention are used in any combination with PYRIMETHAMINE™ and/or LEUCOVORIN™ to prophylactically treat or prevent an opportunistic *Toxoplasma gondii* infection. In another specific embodiment, Therapeutics of the invention are used in any combination with LEUCOVORIN™ and/or NEUPOGEN™ to prophylactically treat or prevent an opportunistic bacterial infection.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antiviral agent. Antiviral agents that may be administered with the Therapeutics of the invention include, but are not limited to, acyclovir, ribavirin, amantadine, and remantidine.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antibiotic agent. Antibiotic agents that may be administered with the Therapeutics of the invention include, but are not limited to, amoxicillin, beta-lactamases, aminoglycosides, beta-lactam (glycopeptide), beta-lactamases, Clindamycin, chloramphenicol, cephalosporins, ciprofloxacin, ciprofloxacin, erythromycin, fluoroquinolones, macrolides, metronidazole, penicillins, quinolones, rifampin, streptomycin, sulfonamide, tetracyclines, trimethoprim, trimethoprim-sulfamthoxazole, and vancomycin.

Conventional nonspecific immunosuppressive agents, that may be administered in combination with the Therapeutics of the invention include, but are not limited to, steroids, cyclosporine, cyclosporine analogs, cyclophosphamide methylprednisone, prednisone,

azathioprine, FK-506, 15-deoxyspergualin, and other immunosuppressive agents that act by suppressing the function of responding T cells.

In specific embodiments, Therapeutics of the invention are administered in combination with immunosuppressants. Immunosuppressants preparations that may be administered with the Therapeutics of the invention include, but are not limited to, ORTHOCLONE™ (OKT3), SANDIMMUNE™/NEORAL™/SANGDYA™ (cyclosporin), PROGRAF™ (tacrolimus), CELLCEPT™ (mycophenolate), Azathioprine, glucorticosteroids, and RAPAMUNE™ (sirolimus). In a specific embodiment, immunosuppressants may be used to prevent rejection of organ or bone marrow transplantation.

In an additional embodiment, Therapeutics of the invention are administered alone or in combination with one or more intravenous immune globulin preparations. Intravenous immune globulin preparations that may be administered with the Therapeutics of the invention include, but not limited to, GAMMAR™, IVEEGAM™, SANDOGLOBULIN™, GAMMAGARD S/D™, and GAMIMUNE™. In a specific embodiment, Therapeutics of the invention are administered in combination with intravenous immune globulin preparations in transplantation therapy (e.g., bone marrow transplant).

In an additional embodiment, the Therapeutics of the invention are administered alone or in combination with an anti-inflammatory agent. Anti-inflammatory agents that may be administered with the Therapeutics of the invention include, but are not limited to, glucocorticoids and the nonsteroidal anti-inflammatories, aminoarylcarboxylic acid derivatives, arylacetic acid derivatives, arylbutyric acid derivatives, arylcarboxylic acids, arylpropionic acid derivatives, pyrazoles, pyrazolones, salicylic acid derivatives, thiazinecarboxamides, e-acetamidocaproic acid, S-adenosylmethionine, 3-amino-4-hydroxybutyric acid, amixetrine, bendazac, benzydamine, bucolome, difenpiramide, ditazol, emorfazone, guaiazulene, nabumetone, nimesulide, orgotein, oxaceprol, paranyline, perisoxal, pifoxime, proquazone, proxazole, and tenidap.

In another embodiment, compostions of the invention are administered in combination with a chemotherapeutic agent. Chemotherapeutic agents that may be administered with the Therapeutics of the invention include, but are not limited to, antibiotic derivatives (e.g., doxorubicin, bleomycin, daunorubicin, and dactinomycin); antiestrogens (e.g., tamoxifen); antimetabolites (e.g., fluorouracil, 5-FU, methotrexate, floxuridine, interferon alpha-2b, glutamic acid, plicamycin, mercaptopurine, and 6-thioguanine);

cytotoxic agents (e.g., carmustine, BCNU, lomustine, CCNU, cytosine arabinoside, cyclophosphamide, estramustine, hydroxyurea, procarbazine, mitomycin, busulfan, cis-platin, and vincristine sulfate); hormones (e.g., medroxyprogesterone, estramustine phosphate sodium, ethinyl estradiol, estradiol, megestrol acetate, methyltestosterone, diethylstilbestrol diphosphate, chlorotrianisene, and testolactone); nitrogen mustard derivatives (e.g., mephalen, chorambucil, mechlorethamine (nitrogen mustard) and thiotepa); steroids and combinations (e.g., bethamethasone sodium phosphate); and others (e.g., dicarbazine, asparaginase, mitotane, vincristine sulfate, vinblastine sulfate, and etoposide).

In a specific embodiment, Therapeutics of the invention are administered in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or any combination of the components of CHOP. In another embodiment, Therapeutics of the invention are administered in combination with Rituximab. In a further embodiment, Therapeutics of the invention are administered with Rituxmab and CHOP, or Rituxmab and any combination of the components of CHOP.

In an additional embodiment, the Therapeutics of the invention are administered in combination with cytokines. Cytokines that may be administered with the Therapeutics of the invention include, but are not limited to, IL2, IL3, IL4, IL5, IL6, IL7, IL10, IL12, IL13, IL15, anti-CD40, CD40L, IFN-gamma and TNF-alpha. In another embodiment, Therapeutics of the invention may be administered with any interleukin, including, but not limited to, IL-1alpha, IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, and IL-21.

In an additional embodiment, the Therapeutics of the invention are administered in combination with angiogenic proteins. Angiogenic proteins that may be administered with the Therapeutics of the invention include, but are not limited to, Glioma Derived Growth Factor (GDGF), as disclosed in European Patent Number EP-399816; Platelet Derived Growth Factor-A (PDGF-A), as disclosed in European Patent Number EP-682110; Platelet Derived Growth Factor-B (PDGF-B), as disclosed in European Patent Number EP-282317; Placental Growth Factor (PlGF), as disclosed in International Publication Number WO 92/06194; Placental Growth Factor-2 (PlGF-2), as disclosed in Hauser et al., Gorwth Factors, 4:259-268 (1993); Vascular Endothelial Growth Factor (VEGF), as disclosed in International Publication Number WO 90/13649; Vascular Endothelial Growth Factor-A (VEGF-A), as disclosed in European Patent Number EP-506477; Vascular Endothelial Growth Factor-2

(VEGF-2), as disclosed in International Publication Number WO 96/39515; Vascular Endothelial Growth Factor B (VEGF-3); Vascular Endothelial Growth Factor B-186 (VEGF-B186), as disclosed in International Publication Number WO 96/26736; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/02543; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/07832; and Vascular Endothelial Growth Factor-E (VEGF-E), as disclosed in German Patent Number DE19639601. The above mentioned references are incorporated herein by reference herein.

In an additional embodiment, the Therapeutics of the invention are administered in combination with hematopoietic growth factors. Hematopoietic growth factors that may be administered with the Therapeutics of the invention include, but are not limited to, LEUKINE™ (SARGRAMOSTIM™) and NEUPOGEN™ (FILGRASTIM™).

In an additional embodiment, the Therapeutics of the invention are administered in combination with Fibroblast Growth Factors. Fibroblast Growth Factors that may be administered with the Therapeutics of the invention include, but are not limited to, FGF-1, FGF-2, FGF-3, FGF-4, FGF-5, FGF-6, FGF-7, FGF-8, FGF-9, FGF-10, FGF-11, FGF-12, FGF-13, FGF-14, and FGF-15.

In additional embodiments, the Therapeutics of the invention are administered in combination with other therapeutic or prophylactic regimens, such as, for example, radiation therapy.

Example 14: Method of Treating Decreased Levels of the Polypeptide

The present invention relates to a method for treating an individual in need of an increased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of an agonist of the invention (including polypeptides of the invention). Moreover, it will be appreciated that conditions caused by a decrease in the standard or normal expression level of a polypeptide of the present invention in an individual can be treated by administering the agonist or antagonist of the present invention. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a Therapeutic comprising an amount of the agonist or

antagonist to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the agonist or antagonist for six consecutive days. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 13.

Example 15: Method of Treating Increased Levels of the Polypeptide

The present invention also relates to a method of treating an individual in need of a decreased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of an antagonist of the invention (including polypeptides and antibodies of the invention).

In one example, antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 13.

Example 16: Method of Treatment Using Gene Therapy-Ex Vivo

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37 degree C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer

is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1 using primers and having appropriate restriction sites and initiation/stop codons, if necessary. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after

having been grown to confluence on cytodex 3 microcarrier beads.

Example 17: Gene Therapy Using Endogenous Genes Corresponding To Polynucleotides of the Invention

Another method of gene therapy according to the present invention involves operably associating the endogenous polynucleotide sequence of the invention with a promoter via homologous recombination as described, for example, in U.S. Patent NO: 5,641,670, issued June 24, 1997; International Publication NO: WO 96/29411, published September 26, 1996; International Publication NO: WO 94/12650, published August 4, 1994; Koller et al., *Proc. Natl. Acad. Sci. USA*, 86:8932-8935 (1989); and Zijlstra et al., *Nature*, 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made which contain a promoter and targeting sequences, which are homologous to the 5' non-coding sequence of endogenous polynucleotide sequence, flanking the promoter. The targeting sequence will be sufficiently near the 5' end of the polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination. The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter.

The amplified promoter and the amplified targeting sequences are digested with the appropriate restriction enzymes and subsequently treated with calf intestinal phosphatase. The digested promoter and digested targeting sequences are added together in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The construct is size fractionated on an agarose gel then purified by phenol extraction and ethanol precipitation.

In this Example, the polynucleotide constructs are administered as naked polynucleotides via electroporation. However, the polynucleotide constructs may also be administered with transfection-facilitating agents, such as liposomes, viral sequences, viral

particles, precipitating agents, etc. Such methods of delivery are known in the art.

Once the cells are transfected, homologous recombination will take place which results in the promoter being operably linked to the endogenous polynucleotide sequence. This results in the expression of polynucleotide corresponding to the polynucleotide in the cell. Expression may be detected by immunological staining, or any other method known in the art.

Fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in DMEM + 10% fetal calf serum. Exponentially growing or early stationary phase fibroblasts are trypsinized and rinsed from the plastic surface with nutrient medium. An aliquot of the cell suspension is removed for counting, and the remaining cells are subjected to centrifugation. The supernatant is aspirated and the pellet is resuspended in 5 ml of electroporation buffer (20 mM HEPES pH 7.3, 137 mM NaCl, 5 mM KCl, 0.7 mM Na_2HPO_4, 6 mM dextrose). The cells are recentrifuged, the supernatant aspirated, and the cells resuspended in electroporation buffer containing 1 mg/ml acetylated bovine serum albumin. The final cell suspension contains approximately $3X10^6$ cells/ml. Electroporation should be performed immediately following resuspension.

Plasmid DNA is prepared according to standard techniques. For example, to construct a plasmid for targeting to the locus corresponding to the polynucleotide of the invention, plasmid pUC18 (MBI Fermentas, Amherst, NY) is digested with HindIII. The CMV promoter is amplified by PCR with an XbaI site on the 5' end and a BamHI site on the 3'end. Two non-coding sequences are amplified via PCR: one non-coding sequence (fragment 1) is amplified with a HindIII site at the 5' end and an Xba site at the 3'end; the other non-coding sequence (fragment 2) is amplified with a BamHI site at the 5'end and a HindIII site at the 3'end. The CMV promoter and the fragments (1 and 2) are digested with the appropriate enzymes (CMV promoter - XbaI and BamHI; fragment 1 - XbaI; fragment 2 - BamHI) and ligated together. The resulting ligation product is digested with HindIII, and ligated with the HindIII-digested pUC18 plasmid.

Plasmid DNA is added to a sterile cuvette with a 0.4 cm electrode gap (Bio-Rad). The final DNA concentration is generally at least 120 μg/ml. 0.5 ml of the cell suspension (containing approximately $1.5.X10^6$ cells) is then added to the cuvette, and the cell suspension and DNA solutions are gently mixed. Electroporation is performed with a Gene-Pulser apparatus (Bio-Rad). Capacitance and voltage are set at 960 μF and 250-300 V,

respectively. As voltage increases, cell survival decreases, but the percentage of surviving cells that stably incorporate the introduced DNA into their genome increases dramatically. Given these parameters, a pulse time of approximately 14-20 mSec should be observed.

Electroporated cells are maintained at room temperature for approximately 5 min, and the contents of the cuvette are then gently removed with a sterile transfer pipette. The cells are added directly to 10 ml of prewarmed nutrient media (DMEM with 15% calf serum) in a 10 cm dish and incubated at 37 degree C. The following day, the media is aspirated and replaced with 10 ml of fresh media and incubated for a further 16-24 hours.

The engineered fibroblasts are then injected into the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads. The fibroblasts now produce the protein product. The fibroblasts can then be introduced into a patient as described above.

Example 18: Method of Treatment Using Gene Therapy - In Vivo

Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide. The polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata et al., Cardiovasc. Res. 35(3):470-479 (1997); Chao et al., Pharmacol. Res. 35(6):517-522 (1997); Wolff, Neuromuscul. Disord. 7(5):314-318 (1997); Schwartz et al., Gene Ther. 3(5):405-411 (1996); Tsurumi et al., Circulation 94(12):3281-3290 (1996) (incorporated herein by reference).

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell,

including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) Ann. NY Acad. Sci. 772:126-139 and Abdallah B. et al. (1995) Biol. Cell 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will

appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

Example 19: Transgenic Animals

The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, *e.g.*, baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (i.e., polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40:691-698 (1994); Carver et al., Biotechnology (NY) 11:1263-1270 (1993); Wright et al., Biotechnology (NY) 9:830-834 (1991); and Hoppe et al., U.S. Pat. No. 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82:6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56:313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3:1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e.g., Ulmer et al., Science 259:1745 (1993); introducing nucleic acid constructs into embryonic pleuripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (Lavitrano et al., Cell 57:717-723 (1989); etc. For a review of such techniques, see Gordon, "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989), which is incorporated by reference herein in its entirety.

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., Nature 380:64-66 (1996); Wilmut et al., Nature 385:810-813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, *i.e.*, mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, *e.g.*, head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci.

USA 89:6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265:103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, *in situ* hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 20: Knock-Out Animals

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (*E.g.*, see Smithies et al., Nature 317:230-234 (1985); Thomas & Capecchi, Cell 51:503-512 (1987); Thompson et al., Cell 5:313-321 (1989); each of which is incorporated by reference herein in its entirety). For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention *in vivo*. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (*e.g.*, see Thomas & Capecchi 1987 and Thompson 1989, *supra*). However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site *in vivo* using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e.g., knockouts) are administered to a patient *in vivo*. Such cells may be obtained from the patient (i.e., animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e.g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered *in vitro* using recombinant DNA techniques to introduce the coding

sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc. The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e.g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, e.g., genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U.S. Patent No. 5,399,349; and Mulligan & Wilson, U.S. Patent No. 5,460,959 each of which is incorporated by reference herein in its entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 22: Assays Detecting Stimulation or Inhibition of B cell Proliferation and Differentiation

Generation of functional humoral immune responses requires both soluble and cognate signaling between B-lineage cells and their microenvironment. Signals may impart a

positive stimulus that allows a B-lineage cell to continue its programmed development, or a negative stimulus that instructs the cell to arrest its current developmental pathway. To date, numerous stimulatory and inhibitory signals have been found to influence B cell responsiveness including IL-2, IL-4, IL-5, IL-6, IL-7, IL10, IL-13, IL-14 and IL-15. Interestingly, these signals are by themselves weak effectors but can, in combination with various co-stimulatory proteins, induce activation, proliferation, differentiation, homing, tolerance and death among B cell populations.

One of the best studied classes of B-cell co-stimulatory proteins is the TNF-superfamily. Within this family CD40, CD27, and CD30 along with their respective ligands CD154, CD70, and CD153 have been found to regulate a variety of immune responses. Assays which allow for the detection and/or observation of the proliferation and differentiation of these B-cell populations and their precursors are valuable tools in determining the effects various proteins may have on these B-cell populations in terms of proliferation and differentiation. Listed below are two assays designed to allow for the detection of the differentiation, proliferation, or inhibition of B-cell populations and their precursors.

In Vitro Assay- Agonists or antagonists of the invention can be assessed for its ability to induce activation, proliferation, differentiation or inhibition and/or death in B-cell populations and their precursors. The activity of the agonists or antagonists of the invention on purified human tonsillar B cells, measured qualitatively over the dose range from 0.1 to 10,000 ng/mL, is assessed in a standard B-lymphocyte co-stimulation assay in which purified tonsillar B cells are cultured in the presence of either formalin-fixed Staphylococcus aureus Cowan I (SAC) or immobilized anti-human IgM antibody as the priming agent. Second signals such as IL-2 and IL-15 synergize with SAC and IgM crosslinking to elicit B cell proliferation as measured by tritiated-thymidine incorporation. Novel synergizing agents can be readily identified using this assay. The assay involves isolating human tonsillar B cells by magnetic bead (MACS) depletion of CD3-positive cells. The resulting cell population is greater than 95% B cells as assessed by expression of CD45R(B220).

Various dilutions of each sample are placed into individual wells of a 96-well plate to which are added 10^5 B-cells suspended in culture medium (RPMI 1640 containing 10% FBS, 5×10^{-5}M 2ME, 100U/ml penicillin, 10ug/ml streptomycin, and 10^{-5} dilution of SAC) in a total volume of 150ul. Proliferation or inhibition is quantitated by a 20h pulse (1uCi/well)

with 3H-thymidine (6.7 Ci/mM) beginning 72h post factor addition. The positive and negative controls are IL2 and medium respectively.

In Vivo Assay- BALB/c mice are injected (i.p.) twice per day with buffer only, or 2 mg/Kg of agonists or antagonists of the invention, or truncated forms thereof. Mice receive this treatment for 4 consecutive days, at which time they are sacrificed and various tissues and serum collected for analyses. Comparison of H&E sections from normal spleens and spleens treated with agonists or antagonists of the invention identify the results of the activity of the agonists or antagonists on spleen cells, such as the diffusion of peri-arterial lymphatic sheaths, and/or significant increases in the nucleated cellularity of the red pulp regions, which may indicate the activation of the differentiation and proliferation of B-cell populations. Immunohistochemical studies using a B cell marker, anti-CD45R(B220), are used to determine whether any physiological changes to splenic cells, such as splenic disorganization, are due to increased B-cell representation within loosely defined B-cell zones that infiltrate established T-cell regions.

Flow cytometric analyses of the spleens from mice treated with agonist or antagonist is used to indicate whether the agonists or antagonists specifically increases the proportion of ThB+, CD45R(B220)dull B cells over that which is observed in control mice.
Likewise, a predicted consequence of increased mature B-cell representation in vivo is a relative increase in serum Ig titers. Accordingly, serum IgM and IgA levels are compared between buffer and agonists or antagonists-treated mice.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 23: T Cell Proliferation Assay

A CD3-induced proliferation assay is performed on PBMCs and is measured by the uptake of ^{3}H-thymidine. The assay is performed as follows. Ninety-six well plates are coated with 100 μl/well of mAb to CD3 (HIT3a, Pharmingen) or isotype-matched control mAb (B33.1) overnight at 4 degrees C (1 μg/ml in .05M bicarbonate buffer, pH 9.5), then washed three times with PBS. PBMC are isolated by F/H gradient centrifugation from human peripheral blood and added to quadruplicate wells (5 x 10^4/well) of mAb coated plates

in RPMI containing 10% FCS and P/S in the presence of varying concentrations of agonists or antagonists of the invention (total volume 200 ul). Relevant protein buffer and medium alone are controls. After 48 hr. culture at 37 degrees C, plates are spun for 2 min. at 1000 rpm and 100 μl of supernatant is removed and stored –20 degrees C for measurement of IL-2 (or other cytokines) if effect on proliferation is observed. Wells are supplemented with 100 ul of medium containing 0.5 uCi of ^{3}H-thymidine and cultured at 37 degrees C for 18-24 hr. Wells are harvested and incorporation of ^{3}H-thymidine used as a measure of proliferation. Anti-CD3 alone is the positive control for proliferation. IL-2 (100 U/ml) is also used as a control which enhances proliferation. Control antibody which does not induce proliferation of T cells is used as the negative controls for the effects of agonists or antagonists of the invention.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 24: Effect of Agonists or Antagonists of the Invention on the Expression of MHC Class II, Costimulatory and Adhesion Molecules and Cell Differentiation of Monocytes and Monocyte-Derived Human Dendritic Cells

Dendritic cells are generated by the expansion of proliferating precursors found in the peripheral blood: adherent PBMC or elutriated monocytic fractions are cultured for 7-10 days with GM-CSF (50 ng/ml) and IL-4 (20 ng/ml). These dendritic cells have the characteristic phenotype of immature cells (expression of CD1, CD80, CD86, CD40 and MHC class II antigens). Treatment with activating factors, such as TNF-α, causes a rapid change in surface phenotype (increased expression of MHC class I and II, costimulatory and adhesion molecules, downregulation of FCγRII, upregulation of CD83). These changes correlate with increased antigen-presenting capacity and with functional maturation of the dendritic cells.

FACS analysis of surface antigens is performed as follows. Cells are treated 1-3 days with increasing concentrations of agonist or antagonist of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degrees C. After an additional wash, the labeled cells are analyzed by flow

cytometry on a FACScan (Becton Dickinson).

Effect on the production of cytokines. Cytokines generated by dendritic cells, in particular IL-12, are important in the initiation of T-cell dependent immune responses. IL-12 strongly influences the development of Thl helper T-cell immune response, and induces cytotoxic T and NK cell function. An ELISA is used to measure the IL-12 release as follows. Dendritic cells (10^6/ml) are treated with increasing concentrations of agonists or antagonists of the invention for 24 hours. LPS (100 ng/ml) is added to the cell culture as positive control. Supernatants from the cell cultures are then collected and analyzed for IL-12 content using commercial ELISA kit (e..g, R & D Systems (Minneapolis, MN)). The standard protocols provided with the kits are used.

Effect on the expression of MHC Class II, costimulatory and adhesion molecules. Three major families of cell surface antigens can be identified on monocytes: adhesion molecules, molecules involved in antigen presentation, and Fc receptor. Modulation of the expression of MHC class II antigens and other costimulatory molecules, such as B7 and ICAM-1, may result in changes in the antigen presenting capacity of monocytes and ability to induce T cell activation. Increase expression of Fc receptors may correlate with improved monocyte cytotoxic activity, cytokine release and phagocytosis.

FACS analysis is used to examine the surface antigens as follows. Monocytes are treated 1-5 days with increasing concentrations of agonists or antagonists of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degreesC. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

Monocyte activation and/or increased survival. Assays for molecules that activate (or alternatively, inactivate) monocytes and/or increase monocyte survival (or alternatively, decrease monocyte survival) are known in the art and may routinely be applied to determine whether a molecule of the invention functions as an inhibitor or activator of monocytes. Agonists or antagonists of the invention can be screened using the three assays described below. For each of these assays, Peripheral blood mononuclear cells (PBMC) are purified

from single donor leukopacks (American Red Cross, Baltimore, MD) by centrifugation through a Histopaque gradient (Sigma). Monocytes are isolated from PBMC by counterflow centrifugal elutriation.

Monocyte Survival Assay. Human peripheral blood monocytes progressively lose viability when cultured in absence of serum or other stimuli. Their death results from internally regulated process (apoptosis). Addition to the culture of activating factors, such as TNF-alpha dramatically improves cell survival and prevents DNA fragmentation. Propidium iodide (PI) staining is used to measure apoptosis as follows. Monocytes are cultured for 48 hours in polypropylene tubes in serum-free medium (positive control), in the presence of 100 ng/ml TNF-alpha (negative control), and in the presence of varying concentrations of the compound to be tested. Cells are suspended at a concentration of 2 x 10^6/ml in PBS containing PI at a final concentration of 5 μg/ml, and then incubaed at room temperature for 5 minutes before FACScan analysis. PI uptake has been demonstrated to correlate with DNA fragmentation in this experimental paradigm.

Effect on cytokine release. An important function of monocytes/macrophages is their regulatory activity on other cellular populations of the immune system through the release of cytokines after stimulation. An ELISA to measure cytokine release is performed as follows. Human monocytes are incubated at a density of $5x10^5$ cells/ml with increasing concentrations of agonists or antagonists of the invention and under the same conditions, but in the absence of agonists or antagonists. For IL-12 production, the cells are primed overnight with IFN (100 U/ml) in presence of agonist or antagonist of the invention. LPS (10 ng/ml) is then added. Conditioned media are collected after 24h and kept frozen until use. Measurement of TNF-alpha, IL-10, MCP-1 and IL-8 is then performed using a commercially available ELISA kit (e. g, R & D Systems (Minneapolis, MN)) and applying the standard protocols provided with the kit.

Oxidative burst. Purified monocytes are plated in 96-w plate at $2\text{-}1x10^5$ cell/well. Increasing concentrations of agonists or antagonists of the invention are added to the wells in a total volume of 0.2 ml culture medium (RPMI 1640 + 10% FCS, glutamine and antibiotics). After 3 days incubation, the plates are centrifuged and the medium is removed from the wells. To

the macrophage monolayers, 0.2 ml per well of phenol red solution (140 mM NaCl, 10 mM potassium phosphate buffer pH 7.0, 5.5 mM dextrose, 0.56 mM phenol red and 19 U/ml of HRPO) is added, together with the stimulant (200 nM PMA). The plates are incubated at 37°C for 2 hours and the reaction is stopped by adding 20 µl 1N NaOH per well. The absorbance is read at 610 nm. To calculate the amount of H_2O_2 produced by the macrophages, a standard curve of a H_2O_2 solution of known molarity is performed for each experiment.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 25: Biological Effects of Agonists or Antagonists of the Invention

Astrocyte and Neuronal Assays.

Agonists or antagonists of the invention, expressed in *Escherichia coli* and purified as described above, can be tested for activity in promoting the survival, neurite outgrowth, or phenotypic differentiation of cortical neuronal cells and for inducing the proliferation of glial fibrillary acidic protein immunopositive cells, astrocytes. The selection of cortical cells for the bioassay is based on the prevalent expression of FGF-1 and FGF-2 in cortical structures and on the previously reported enhancement of cortical neuronal survival resulting from FGF-2 treatment. A thymidine incorporation assay, for example, can be used to elucidate an agonist or antagonist of the invention's activity on these cells.

Moreover, previous reports describing the biological effects of FGF-2 (basic FGF) on cortical or hippocampal neurons *in vitro* have demonstrated increases in both neuron survival and neurite outgrowth (Walicke et al., "Fibroblast growth factor promotes survival of dissociated hippocampal neurons and enhances neurite extension." *Proc. Natl. Acad. Sci. USA 83*:3012-3016. (1986), assay herein incorporated by reference in its entirety). However, reports from experiments done on PC-12 cells suggest that these two responses are not necessarily synonymous and may depend on not only which FGF is being tested but also on which receptor(s) are expressed on the target cells. Using the primary cortical neuronal

culture paradigm, the ability of an agonist or antagonist of the invention to induce neurite outgrowth can be compared to the response achieved with FGF-2 using, for example, a thymidine incorporation assay.

Fibroblast and endothelial cell assays.

Human lung fibroblasts are obtained from Clonetics (San Diego, CA) and maintained in growth media from Clonetics. Dermal microvascular endothelial cells are obtained from Cell Applications (San Diego, CA). For proliferation assays, the human lung fibroblasts and dermal microvascular endothelial cells can be cultured at 5,000 cells/well in a 96-well plate for one day in growth medium. The cells are then incubated for one day in 0.1% BSA basal medium. After replacing the medium with fresh 0.1% BSA medium, the cells are incubated with the test proteins for 3 days. Alamar Blue (Alamar Biosciences, Sacramento, CA) is added to each well to a final concentration of 10%. The cells are incubated for 4 hr. Cell viability is measured by reading in a CytoFluor fluorescence reader. For the PGE_2 assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or agonists or antagonists of the invention with or without IL-1α for 24 hours. The supernatants are collected and assayed for PGE_2 by EIA kit (Cayman, Ann Arbor, MI). For the IL-6 assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or with or without agonists or antagonists of the invention IL-1α for 24 hours. The supernatants are collected and assayed for IL-6 by ELISA kit (Endogen, Cambridge, MA).

Human lung fibroblasts are cultured with FGF-2 or agonists or antagonists of the invention for 3 days in basal medium before the addition of Alamar Blue to assess effects on growth of the fibroblasts. FGF-2 should show a stimulation at 10 - 2500 ng/ml which can be used to compare stimulation with agonists or antagonists of the invention.

Parkinson Models.

The loss of motor function in Parkinson's disease is attributed to a deficiency of striatal dopamine resulting from the degeneration of the nigrostriatal dopaminergic projection

neurons. An animal model for Parkinson's that has been extensively characterized involves the systemic administration of 1-methyl-4 phenyl 1,2,3,6-tetrahydropyridine (MPTP). In the CNS, MPTP is taken-up by astrocytes and catabolized by monoamine oxidase B to 1-methyl-4-phenyl pyridine (MPP^+) and released. Subsequently, MPP^+ is actively accumulated in dopaminergic neurons by the high-affinity reuptake transporter for dopamine. MPP^+ is then concentrated in mitochondria by the electrochemical gradient and selectively inhibits nicotidamide adenine disphosphate: ubiquinone oxidoreductionase (complex I), thereby interfering with electron transport and eventually generating oxygen radicals.

It has been demonstrated in tissue culture paradigms that FGF-2 (basic FGF) has trophic activity towards nigral dopaminergic neurons (Ferrari et al., Dev. Biol. 1989). Recently, Dr. Unsicker's group has demonstrated that administering FGF-2 in gel foam implants in the striatum results in the near complete protection of nigral dopaminergic neurons from the toxicity associated with MPTP exposure (Otto and Unsicker, J. Neuroscience, 1990).

Based on the data with FGF-2, agonists or antagonists of the invention can be evaluated to determine whether it has an action similar to that of FGF-2 in enhancing dopaminergic neuronal survival *in vitro* and it can also be tested *in vivo* for protection of dopaminergic neurons in the striatum from the damage associated with MPTP treatment. The potential effect of an agonist or antagonist of the invention is first examined in vitro in a dopaminergic neuronal cell culture paradigm. The cultures are prepared by dissecting the midbrain floor plate from gestation day 14 Wistar rat embryos. The tissue is dissociated with trypsin and seeded at a density of 200,000 cells/cm^2 on polyorthinine-laminin coated glass coverslips. The cells are maintained in Dulbecco's Modified Eagle's medium and F12 medium containing hormonal supplements (N1). The cultures are fixed with paraformaldehyde after 8 days in vitro and are processed for tyrosine hydroxylase, a specific marker for dopminergic neurons, immunohistochemical staining. Dissociated cell cultures are prepared from embryonic rats. The culture medium is changed every third day and the factors are also added at that time.

Since the dopaminergic neurons are isolated from animals at gestation day 14, a developmental time which is past the stage when the dopaminergic precursor cells are proliferating, an increase in the number of tyrosine hydroxylase immunopositive neurons would represent an increase in the number of dopaminergic neurons surviving *in vitro*.

Therefore, if an agonist or antagonist of the invention acts to prolong the survival of dopaminergic neurons, it would suggest that the agonist or antagonist may be involved in Parkinson's Disease.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 26: The Effect of Agonists or Antagonists of the Invention on the Growth of Vascular Endothelial Cells

On day 1, human umbilical vein endothelial cells (HUVEC) are seeded at 2-5x10^4 cells/35 mm dish density in M199 medium containing 4% fetal bovine serum (FBS), 16 units/ml heparin, and 50 units/ml endothelial cell growth supplements (ECGS, Biotechnique, Inc.). On day 2, the medium is replaced with M199 containing 10% FBS, 8 units/ml heparin. An agonist or antagonist of the invention, and positive controls, such as VEGF and basic FGF (bFGF) are added, at varying concentrations. On days 4 and 6, the medium is replaced. On day 8, cell number is determined with a Coulter Counter.

An increase in the number of HUVEC cells indicates that the compound of the invention may proliferate vascular endothelial cells, while a decrease in the number of HUVEC cell indicates that the compound of the invention inhibits vascular endothelial cells.

The studies described in this example tested activity of a polypeptide of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), agonists, and/or antagonists of the invention.

Example 27: Rat Corneal Wound Healing Model

This animal model shows the effect of an agonist or antagonist of the invention on neovascularization. The experimental protocol includes:

a) Making a 1-1.5 mm long incision from the center of cornea into the stromal layer.

b) Inserting a spatula below the lip of the incision facing the outer corner of the

eye.

c) Making a pocket (its base is 1-1.5 mm form the edge of the eye).

d) Positioning a pellet, containing 50ng- 5ug of an agonist or antagonist of the invention, within the pocket.

e) Treatment with an agonist or antagonist of the invention can also be applied topically to the corneal wounds in a dosage range of 20mg - 500mg (daily treatment for five days).

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 28: Diabetic Mouse and Glucocorticoid-Impaired Wound Healing Models

A. Diabetic db+/db+ Mouse Model.

To demonstrate that an agonist or antagonist of the invention accelerates the healing process, the genetically diabetic mouse model of wound healing is used. The full thickness wound healing model in the db+/db+ mouse is a well characterized, clinically relevant and reproducible model of impaired wound healing. Healing of the diabetic wound is dependent on formation of granulation tissue and re-epithelialization rather than contraction (Gartner, M.H. *et al., J. Surg. Res. 52*:389 (1992); Greenhalgh, D.G. *et al., Am. J. Pathol. 136*:1235 (1990)).

The diabetic animals have many of the characteristic features observed in Type II diabetes mellitus. Homozygous (db+/db+) mice are obese in comparison to their normal heterozygous (db+/+m) littermates. Mutant diabetic (db+/db+) mice have a single autosomal recessive mutation on chromosome 4 (db+) (Coleman *et al. Proc. Natl. Acad. Sci. USA 77*:283-293 (1982)). Animals show polyphagia, polydipsia and polyuria. Mutant diabetic mice (db+/db+) have elevated blood glucose, increased or normal insulin levels, and suppressed cell-mediated immunity (Mandel *et al., J. Immunol. 120*:1375 (1978); Debray-Sachs, M. *et al., Clin. Exp. Immunol. 51(1)*:1-7 (1983); Leiter *et al., Am. J. of Pathol. 114*:46-55 (1985)). Peripheral neuropathy, myocardial complications, and microvascular lesions, basement membrane thickening and glomerular filtration abnormalities have been described in these animals (Norido, F. *et al., Exp. Neurol. 83(2)*:221-232 (1984); Robertson *et al.*,

Diabetes 29(1):60-67 (1980); Giacomelli *et al.*. *Lab Invest. 40(4)*:460-473 (1979); Coleman, D.L., *Diabetes 31 (Suppl)*:1-6 (1982)). These homozygous diabetic mice develop hyperglycemia that is resistant to insulin analogous to human type II diabetes (Mandel *et al.*, *J. Immunol. 120*:1375-1377 (1978)).

The characteristics observed in these animals suggests that healing in this model may be similar to the healing observed in human diabetes (Greenhalgh, *et al.*, *Am. J. of Pathol. 136*:1235-1246 (1990)).

Genetically diabetic female C57BL/KsJ (db+/db+) mice and their non-diabetic (db+/+m) heterozygous littermates are used in this study (Jackson Laboratories). The animals are purchased at 6 weeks of age and are 8 weeks old at the beginning of the study. Animals are individually housed and received food and water ad libitum. All manipulations are performed using aseptic techniques. The experiments are conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

Wounding protocol is performed according to previously reported methods (Tsuboi, R. and Rifkin, D.B., *J. Exp. Med. 172*:245-251 (1990)). Briefly, on the day of wounding, animals are anesthetized with an intraperitoneal injection of Avertin (0.01 mg/mL), 2,2,2-tribromoethanol and 2-methyl-2-butanol dissolved in deionized water. The dorsal region of the animal is shaved and the skin washed with 70% ethanol solution and iodine. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is then created using a Keyes tissue punch. Immediately following wounding, the surrounding skin is gently stretched to eliminate wound expansion. The wounds are left open for the duration of the experiment. Application of the treatment is given topically for 5 consecutive days commencing on the day of wounding. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

Wounds are visually examined and photographed at a fixed distance at the day of surgery and at two day intervals thereafter. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

An agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups

received 50mL of vehicle solution.

Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology and immunohistochemistry. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

Three groups of 10 animals each (5 diabetic and 5 non-diabetic controls) are evaluated: 1) Vehicle placebo control, 2) untreated group, and 3) treated group.

Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total square area of the wound. Contraction is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is $64mm^2$, the corresponding size of the dermal punch. Calculations are made using the following formula:

[Open area on day 8] - [Open area on day 1] / [Open area on day 1]

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using a Reichert-Jung microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds are used to assess whether the healing process and the morphologic appearance of the repaired skin is altered by treatment with an agonist or antagonist of the invention. This assessment included verification of the presence of cell accumulation, inflammatory cells, capillaries, fibroblasts, re-epithelialization and epidermal maturity (Greenhalgh, D.G. *et al., Am. J. Pathol. 136:*1235 (1990)). A calibrated lens micrometer is used by a blinded observer.

Tissue sections are also stained immunohistochemically with a polyclonal rabbit anti-human keratin antibody using ABC Elite detection system. Human skin is used as a positive tissue control while non-immune IgG is used as a negative control. Keratinocyte growth is determined by evaluating the extent of reepithelialization of the wound using a calibrated lens micrometer.

Proliferating cell nuclear antigen/cyclin (PCNA) in skin specimens is demonstrated by using anti-PCNA antibody (1:50) with an ABC Elite detection system. Human colon cancer served as a positive tissue control and human brain tissue is used as a negative tissue

control. Each specimen included a section with omission of the primary antibody and substitution with non-immune mouse IgG. Ranking of these sections is based on the extent of proliferation on a scale of 0-8, the lower side of the scale reflecting slight proliferation to the higher side reflecting intense proliferation.

Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

B. Steroid Impaired Rat Model

The inhibition of wound healing by steroids has been well documented in various *in vitro* and *in vivo* systems (Wahl, Glucocorticoids and Wound healing. In: Anti-Inflammatory Steroid Action: Basic and Clinical Aspects. 280-302 (1989); Wahl*et al., J. Immunol. 115*: 476-481 (1975); Werb *et al., J. Exp. Med. 147*:1684-1694 (1978)). Glucocorticoids retard wound healing by inhibiting angiogenesis, decreasing vascular permeability (Ebert *et al., An. Intern. Med. 37*:701-705 (1952)), fibroblast proliferation, and collagen synthesis (Beck *et al., Growth Factors. 5:* 295-304 (1991); Haynes *et al., J. Clin. Invest. 61:* 703-797 (1978)) and producing a transient reduction of circulating monocytes (Haynes et al., *J. Clin. Invest. 61:* 703-797 (1978); Wahl, "Glucocorticoids and wound healing", *In:* Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989)). The systemic administration of steroids to impaired wound healing is a well establish phenomenon in rats (Beck *et al., Growth Factors. 5:* 295-304 (1991); Haynes *et al., J. Clin. Invest. 61:* 703-797 (1978); Wahl, "Glucocorticoids and wound healing", *In*: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989); Pierce *et al., Proc. Natl. Acad. Sci. USA 86*: 2229-2233 (1989)).

To demonstrate that an agonist or antagonist of the invention can accelerate the healing process, the effects of multiple topical applications of the agonist or antagonist on full thickness excisional skin wounds in rats in which healing has been impaired by the systemic administration of methylprednisolone is assessed.

Young adult male Sprague Dawley rats weighing 250-300 g (Charles River Laboratories) are used in this example. The animals are purchased at 8 weeks of age and are 9 weeks old at the beginning of the study. The healing response of rats is impaired by the systemic administration of methylprednisolone (17mg/kg/rat intramuscularly) at the time of wounding. Animals are individually housed and received food and water *ad libitum*. All

manipulations are performed using aseptic techniques. This study is conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

The wounding protocol is followed according to section A, above. On the day of wounding, animals are anesthetized with an intramuscular injection of ketamine (50 mg/kg) and xylazine (5 mg/kg). The dorsal region of the animal is shaved and the skin washed with 70% ethanol and iodine solutions. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is created using a Keyes tissue punch. The wounds are left open for the duration of the experiment. Applications of the testing materials are given topically once a day for 7 consecutive days commencing on the day of wounding and subsequent to methylprednisolone administration. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

Wounds are visually examined and photographed at a fixed distance at the day of wounding and at the end of treatment. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

The agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

Four groups of 10 animals each (5 with methylprednisolone and 5 without glucocorticoid) are evaluated: 1) Untreated group 2) Vehicle placebo control 3) treated groups.

Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total area of the wound. Closure is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is $64mm^2$, the corresponding size of the dermal punch. Calculations are made using the following formula:

[Open area on day 8] - [Open area on day 1] / [Open area on day 1]

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using an Olympus microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds allows assessment of whether the healing process and the morphologic appearance of the repaired skin is improved by treatment with an agonist or antagonist of the invention. A calibrated lens micrometer is used by a blinded observer to determine the distance of the wound gap.

Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 29: Lymphadema Animal Model

The purpose of this experimental approach is to create an appropriate and consistent lymphedema model for testing the therapeutic effects of an agonist or antagonist of the invention in lymphangiogenesis and re-establishment of the lymphatic circulatory system in the rat hind limb. Effectiveness is measured by swelling volume of the affected limb, quantification of the amount of lymphatic vasculature, total blood plasma protein, and histopathology. Acute lymphedema is observed for 7-10 days. Perhaps more importantly, the chronic progress of the edema is followed for up to 3-4 weeks.

Prior to beginning surgery, blood sample is drawn for protein concentration analysis. Male rats weighing approximately ~350g are dosed with Pentobarbital. Subsequently, the right legs are shaved from knee to hip. The shaved area is swabbed with gauze soaked in 70% EtOH. Blood is drawn for serum total protein testing. Circumference and volumetric measurements are made prior to injecting dye into paws after marking 2 measurement levels (0.5 cm above heel, at mid-pt of dorsal paw). The intradermal dorsum of both right and left paws are injected with 0.05 ml of 1% Evan's Blue. Circumference and volumetric

measurements are then made following injection of dye into paws.

Using the knee joint as a landmark. a mid-leg inguinal incision is made circumferentially allowing the femoral vessels to be located. Forceps and hemostats are used to dissect and separate the skin flaps. After locating the femoral vessels, the lymphatic vessel that runs along side and underneath the vessel(s) is located. The main lymphatic vessels in this area are then electrically coagulated or suture ligated.

Using a microscope, muscles in back of the leg (near the semitendinosis and adductors) are bluntly dissected. The popliteal lymph node is then located. The 2 proximal and 2 distal lymphatic vessels and distal blood supply of the popliteal node are then and ligated by suturing. The popliteal lymph node, and any accompanying adipose tissue, is then removed by cutting connective tissues.

Care is taken to control any mild bleeding resulting from this procedure. After lymphatics are occluded, the skin flaps are sealed by using liquid skin (Vetbond) (AJ Buck). The separated skin edges are sealed to the underlying muscle tissue while leaving a gap of ~0.5 cm around the leg. Skin also may be anchored by suturing to underlying muscle when necessary.

To avoid infection, animals are housed individually with mesh (no bedding). Recovering animals are checked daily through the optimal edematous peak, which typically occurred by day 5-7. The plateau edematous peak are then observed. To evaluate the intensity of the lymphedema, the circumference and volumes of 2 designated places on each paw before operation and daily for 7 days are measured. The effect plasma proteins on lymphedema is determined and whether protein analysis is a useful testing perimeter is also investigated. The weights of both control and edematous limbs are evaluated at 2 places. Analysis is performed in a blind manner.

Circumference Measurements: Under brief gas anesthetic to prevent limb movement, a cloth tape is used to measure limb circumference. Measurements are done at the ankle bone and dorsal paw by 2 different people then those 2 readings are averaged. Readings are taken from both control and edematous limbs.

Volumetric Measurements: On the day of surgery, animals are anesthetized with Pentobarbital and are tested prior to surgery. For daily volumetrics animals are under brief halothane anesthetic (rapid immobilization and quick recovery), both legs are shaved and equally marked using waterproof marker on legs. Legs are first dipped in water, then dipped

into instrument to each marked level then measured by Buxco edema software(Chen/Victor). Data is recorded by one person, while the other is dipping the limb to marked area.

Blood-plasma protein measurements: Blood is drawn, spun, and serum separated prior to surgery and then at conclusion for total protein and Ca2+ comparison.

Limb Weight Comparison: After drawing blood, the animal is prepared for tissue collection. The limbs are amputated using a quillitine, then both experimental and control legs are cut at the ligature and weighed. A second weighing is done as the tibio-cacaneal joint is disarticulated and the foot is weighed.

Histological Preparations: The transverse muscle located behind the knee (popliteal) area is dissected and arranged in a metal mold, filled with freezeGel, dipped into cold methylbutane, placed into labeled sample bags at - 80EC until sectioning. Upon sectioning, the muscle is observed under fluorescent microscopy for lymphatics..

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 30: Suppression of TNF alpha-induced adhesion molecule expression by a Agonist or Antagonist of the Invention

The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

Tumor necrosis factor alpha (TNF-a), a potent proinflammatory cytokine, is a stimulator of all three CAMs on endothelial cells and may be involved in a wide variety of inflammatory responses, often resulting in a pathological outcome.

The potential of an agonist or antagonist of the invention to mediate a suppression of TNF-a induced CAM expression can be examined. A modified ELISA assay which uses ECs as a solid phase absorbent is employed to measure the amount of CAM expression on TNF-a treated ECs when co-stimulated with a member of the FGF family of proteins.

To perform the experiment, human umbilical vein endothelial cell (HUVEC) cultures are obtained from pooled cord harvests and maintained in growth medium (EGM-2; Clonetics, San Diego, CA) supplemented with 10% FCS and 1% penicillin/streptomycin in a 37 degree C humidified incubator containing 5% CO_2. HUVECs are seeded in 96-well plates at concentrations of 1×10^4 cells/well in EGM medium at 37 degree C for 18-24 hrs or until confluent. The monolayers are subsequently washed 3 times with a serum-free solution of RPMI-1640 supplemented with 100 U/ml penicillin and 100 mg/ml streptomycin, and treated with a given cytokine and/or growth factor(s) for 24 h at 37 degree C. Following incubation, the cells are then evaluated for CAM expression.

Human Umbilical Vein Endothelial cells (HUVECs) are grown in a standard 96 well plate to confluence. Growth medium is removed from the cells and replaced with 90 ul of 199 Medium (10% FBS). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 ul volumes). Plates are incubated at 37 degree C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 µl of 0.1% paraformaldehyde-PBS(with Ca++ and Mg++) is added to each well. Plates are held at 4°C for 30 min.

Fixative is then removed from the wells and wells are washed 1X with PBS(+Ca,Mg)+0.5% BSA and drained. Do not allow the wells to dry. Add 10 µl of diluted primary antibody to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 µg/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA.

Then add 20 µl of diluted ExtrAvidin-Alkaline Phosphotase (1:5,000 dilution) to each well and incubated at 37°C for 30 min. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA. 1 tablet of p-Nitrophenol Phosphate pNPP is dissolved in 5 ml of glycine buffer (pH 10.4). 100 µl of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphotase in glycine buffer: 1:5,000 (10^0) > $10^{-0.5}$ > 10^{-1} > $10^{-1.5}$. 5 µl of each dilution is added to triplicate

wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 µl of pNNP reagent must then be added to each of the standard wells. The plate must be incubated at 37°C for 4h. A volume of 50 µl of 3M NaOH is added to all wells. The results are quantified on a plate reader at 405 nm. The background subtraction option is used on blank wells filled with glycine buffer only. The template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 31: Production Of Polypeptide of the Invention For High-Throughput Screening Assays

The following protocol produces a supernatant containing polypeptide of the present invention to be tested. This supernatant can then be used in the Screening Assays described in Examples 33-42.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at 2 x 10^5 cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing

a polynucleotide insert, produced by the methods described in Examples 8-10, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37 degree C for 6 hours.

While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or HGS CHO-5 media (116.6 mg/L of CaCl2 (anhyd); 0.00130 mg/L $CuSO_4$-$5H_2O$; 0.050 mg/L of $Fe(NO_3)_3$-$9H_2O$; 0.417 mg/L of $FeSO_4$-$7H_2O$; 311.80 mg/L of Kcl; 28.64 mg/L of $MgCl_2$; 48.84 mg/L of $MgSO_4$; 6995.50 mg/L of NaCl; 2400.0 mg/L of $NaHCO_3$; 62.50 mg/L of NaH_2PO_4-H_20; 71.02 mg/L of Na_2HPO4; .4320 mg/L of $ZnSO_4$-$7H_2O$; .002 mg/L of Arachidonic Acid ; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine-H_20; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL-H_20; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL-H_20; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalainine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tryrosine-2Na-$2H_20$; and 99.65 mg/ml of L-

Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; 0.680 mg/L of Vitamin B_{12}; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal Acetate. Adjust osmolarity to 327 mOsm) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml appropriate media to each well. Incubate at 37 degree C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 33-40.

It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide of the present invention directly (e.g., as a secreted protein) or by polypeptide of the present invention inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity in a particular assay.

Example 32: Construction of GAS Reporter Construct

One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements

alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types. as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:838)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

Ligand	JAKs tyk2	Jak1	Jak2	Jak3	STATS	GAS(elements) or ISRE
IFN family						
IFN-a/B	+	+	-	-	1,2,3	ISRE
IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
Il-10	+	?	?	-	1,3	
gp130 family						
IL-6 (Pleiotrohic)	+	+	+	?	1,3	GAS (IRF1>Lys6>IFP)
Il-11(Pleiotrohic)	?	+	?	?	1,3	
OnM(Pleiotrohic)	?	+	+	?	1,3	
LIF(Pleiotrohic)	?	+	+	?	1,3	
CNTF(Pleiotrohic)	-/+	+	+	?	1,3	
G-CSF(Pleiotrohic)	?	+	?	?	1,3	
IL-12(Pleiotrohic)	+	-	+	+	1,3	
g-C family						
IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP >>Ly6)(IgH)
IL-7 (lymphocytes)	-	+	-	+	5	GAS
IL-9 (lymphocytes)	-	+	-	+	5	GAS
IL-13 (lymphocyte)	-	+	?	?	6	GAS
IL-15	?	+	?	+	5	GAS
gp140 family						
IL-3 (myeloid)	-	-	+	-	5	GAS (IRF1>IFP>>Ly6)
IL-5 (myeloid)	-	-	+	-	5	GAS
GM-CSF (myeloid)	-	-	+	-	5	GAS
Growth hormone family						
GH	?	-	+	-	5	
PRL	?	+/-	+	-	1,3,5	
EPO	?	-	+	-	5	GAS(B-

CAS>IRF1=IFP>>Ly6)

Receptor Tyrosine Kinases

EGF	?	+	+	-	1,3	GAS (IRF1)
PDGF	?	+	+	-	1,3	
CSF-1	?	+	+	-	1,3	GAS (not IRF1)

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 33-34, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

5':GCGCCTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCC GAAATGATTTCCCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:839)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:840)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAA TGATTTCCCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCG CCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCT CCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCC TCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTA GGCTTTTGCAAAAAGCTT:3' (SEQ ID NO:841)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol

acetyltransferase (CAT), luciferase. alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 33-34.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 35 and 36. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, Il-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

Example 33: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, and determining whether supernate containing a polypeptide of the invention proliferates and/or differentiates T-cells. T-cell activity is assessed using the

GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml genticin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies) with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells (10^7 per transfection), and resuspend in OPTI-MEM to a final concentration of 10^7 cells/ml. Then add 1ml of 1 x 10^7 cells in OPTI-MEM to T25 flask and incubate at 37 degree C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Genticin, and 1% Pen-Strep. These cells are treated with supernatants containing polypeptide of the present invention or polypeptide of the present invention induced polypeptides as produced by the protocol described in Example 31.

On the day of treatment with the supernatant, the cells should be washed and

resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20 degree C until SEAP assays are performed according to Example 37. The plates containing the remaining treated cells are placed at 4 degree C and serve as a source of material for repeating the assay on a specific well if desired.

As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

The above protocol may be used in the generation of both transient, as well as, stable transfected cells, which would be apparent to those of skill in the art.

Example 34: High-Throughput Screening Assay Identifying Myeloid Activity

The following protocol is used to assess myeloid activity of polypeptide of the present invention by determining whether polypeptide of the present invention proliferates and/or differentiates myeloid cells. Myeloid cell activity is assessed using

the GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 32, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2x10e^7 U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM $Na_2HPO_4.7H_2O$, 1 mM $MgCl_2$, and 675 uM $CaCl_2$. Incubate at 37 degrees C for 45 min.

Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37 degree C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

These cells are tested by harvesting $1x10^8$ cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of $5x10^5$ cells/ml. Plate 200 ul cells per well in the 96-well plate (or $1x10^5$ cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example 31. Incubate at 37 degee C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 37.

Example 35: High-Throughput Screening Assay Identifying Neuronal Activity.

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed by polypeptide of the present invention.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells by polypeptide of the present invention can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:842)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:843)

Using the GAS:SEAP/Neo vector produced in Example 32, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and

allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 31. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as $5x10^5$ cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to $1x10^5$ cells/well). Add 50 ul supernatant produced by Example 31, 37 degree C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 37.

Example 36: High-Throughput Screening Assay for T-cell Activity

NF-KB (Nuclear Factor KB) is a transcription factor activated by a wide

variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-KB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- KB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- KB is retained in the cytoplasm with I-KB (Inhibitor KB). However, upon stimulation, I- KB is phosphorylated and degraded, causing NF- KB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- KB include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-KB promoter element are used to screen the supernatants produced in Example 31. Activators or inhibitors of NF-KB would be useful in treating, preventing, and/or diagnosing diseases. For example, inhibitors of NF-KB could be used to treat those diseases related to the acute or chronic activation of NF-KB, such as rheumatoid arthritis.

To construct a vector containing the NF-KB promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF-KB binding site (GGGGACTTTCCC) (SEQ ID NO:844), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:845)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:840)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene)

Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCC ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCC ATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGA CTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTA TTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAA GCTT:3' (SEQ ID NO:846)

Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF-KB/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF-KB/SV40/SEAP cassette is removed from the above NF-KB/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the NF-KB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

Once NF-KB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 33. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described in Example 33. As a positive control, exogenous TNF alpha (0.1,1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

Example 37: Assay for SEAP Activity

As a reporter molecule for the assays described in Examples 33-36, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 ul of 2.5x

dilution buffer into Optiplates containing 35 ul of a supernatant. Seal the plates with a plastic sealer and incubate at 65 degree C for 30 min. Separate the Optiplates to avoid uneven heating.

Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 ml Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 ul Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

Reaction Buffer Formulation:

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6
23	125	6.25

24	130	6.5
25	135	6.75
26	140	7
27	145	7.25
28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

Example 38: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-4 (Molecular Probes, Inc.; catalog no. F-14202), used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO_2 incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-4 is made in 10% pluronic acid DMSO. To load the cells with fluo-4 , 50 ul of 12 ug/ml fluo-4 is added to each well. The plate is incubated at 37 degrees C in a CO_2 incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10^6 cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-4 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37 degrees C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10^6 cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley Cell Wash with 200 ul, followed by an aspiration step to 100 ul final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as

fluo-4 . The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event caused by the a molecule, either polypeptide of the present invention or a molecule induced by polypeptide of the present invention, which has resulted in an increase in the intracellular Ca^{++} concentration.

Example 40: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, identifying whether polypeptide of the present invention or a molecule induced by polypeptide of the present invention is capable of activating tyrosine kinase signal transduction pathways is of interest. Therefore, the following protocol

is designed to identify such molecules capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford,MA), or calf serum, rinsed with PBS and stored at 4 degree C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford,MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 31, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na3VO4, 2 mM Na4P2O7 and a cocktail of protease inhibitors (# 1836170) obtained from Boeheringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4^{o}C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4

degree C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg_{2+} (5mM ATP/50mM $MgCl_2$), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM $MgCl_2$, 5 mM $MnCl_2$, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30 degree C for 2 min. Initial the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mm EDTA and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37 degree C for 20 min. This allows the streptavadin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phospotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37 degree C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of

tyrosine kinase activity.

Example 41: High-Throughput Screening Assay Identifying Phosphorylation Activity

As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 40, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4 degree C until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 31 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the

Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation by polypeptide of the present invention or a molecule induced by polypeptide of the present invention.

Example 42: Assay for the Stimulation of Bone Marrow CD34+ Cell Proliferation

This assay is based on the ability of human CD34+ to proliferate in the presence of hematopoietic growth factors and evaluates the ability of isolated polypeptides expressed in mammalian cells to stimulate proliferation of CD34+ cells.

It has been previously shown that most mature precursors will respond to only a single signal. More immature precursors require at least two signals to respond. Therefore, to test the effect of polypeptides on hematopoietic activity of a wide range of progenitor cells, the assay contains a given polypeptide in the presence or absence of other hematopoietic growth factors. Isolated cells are cultured for 5 days in the presence of Stem Cell Factor (SCF) in combination with tested sample. SCF alone has a very limited effect on the proliferation of bone marrow (BM) cells, acting in such conditions only as a "survival" factor. However, combined with any factor exhibiting stimulatory effect on these cells (e.g., IL-3), SCF will cause a synergistic effect. Therefore, if the tested polypeptide has a stimulatory effect on a hematopoietic progenitors, such activity can be easily detected. Since normal BM cells have a low level of cycling cells, it is likely that any inhibitory effect of a given polypeptide, or agonists or antagonists thereof, might not be detected. Accordingly, assays for an inhibitory effect on progenitors is preferably tested in cells that are first subjected to *in vitro* stimulation with SCF+IL+3, and then contacted with the compound that is being evaluated for inhibition of such induced proliferation.

Briefly, CD34+ cells are isolated using methods known in the art. The cells are thawed and resuspended in medium (QBSF 60 serum-free medium with 1% L-

glutamine (500ml) Quality Biological. Inc., Gaithersburg, MD Cat# 160-204-101). After several gentle centrifugation steps at 200 x g, cells are allowed to rest for one hour. The cell count is adjusted to 2.5 x 10^5 cells/ml. During this time, 100 μl of sterile water is added to the peripheral wells of a 96-well plate. The cytokines that can be tested with a given polypeptide in this assay is rhSCF (R&D Systems, Minneapolis, MN, Cat# 255-SC) at 50 ng/ml alone and in combination with rhSCF and rhIL-3 (R&D Systems, Minneapolis, MN, Cat# 203-ML) at 30 ng/ml. After one hour, 10 μl of prepared cytokines, 50 μl of the supernatants prepared in Example 31 (supernatants at 1:2 dilution = 50 μl) and 20 μl of diluted cells are added to the media which is already present in the wells to allow for a final total volume of 100 μl. The plates are then placed in a 37°C/5% CO_2 incubator for five days.

Eighteen hours before the assay is harvested, 0.5 μCi/well of [3H] Thymidine is added in a 10 μl volume to each well to determine the proliferation rate. The experiment is terminated by harvesting the cells from each 96-well plate to a filtermat using the Tomtec Harvester 96. After harvesting, the filtermats are dried, trimmed and placed into OmniFilter assemblies consisting of one OmniFilter plate and one OmniFilter Tray. 60 μl Microscint is added to each well and the plate sealed with TopSeal-A press-on sealing film A bar code 15 sticker is affixed to the first plate for counting. The sealed plates is then loaded and the level of radioactivity determined via the Packard Top Count and the printed data collected for analysis. The level of radioactivity reflects the amount of cell proliferation.

The studies described in this example test the activity of a given polypeptide to stimulate bone marrow CD34+ cell proliferation. One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof. As a nonlimiting example, potential antagonists tested in this assay would be expected to inhibit cell proliferation in the presence of cytokines and/or to increase the inhibition of cell proliferation in the presence of cytokines and a given polypeptide. In contrast, potential agonists tested in this assay would be expected to enhance cell proliferation and/or to decrease the inhibition of cell proliferation in the presence of

cytokines and a given polypeptide.

The ability of a gene to stimulate the proliferation of bone marrow CD34+ cells indicates that polynucleotides and polypeptides corresponding to the gene are useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein.

Example 43: Assay for Extracellular Matrix Enhanced Cell Response (EMECR)

The objective of the Extracellular Matrix Enhanced Cell Response (EMECR) assay is to identify gene products (e.g., isolated polypeptides) that act on the hematopoietic stem cells in the context of the extracellular matrix (ECM) induced signal.

Cells respond to the regulatory factors in the context of signal(s) received from the surrounding microenvironment. For example, fibroblasts, and endothelial and epithelial stem cells fail to replicate in the absence of signals from the ECM. Hematopoietic stem cells can undergo self-renewal in the bone marrow, but not in *in vitro* suspension culture. The ability of stem cells to undergo self-renewal *in vitro* is dependent upon their interaction with the stromal cells and the ECM protein fibronectin (fn). Adhesion of cells to fn is mediated by the $\alpha_5.\beta_1$ and $\alpha_4.\beta_1$ integrin receptors, which are expressed by human and mouse hematopoietic stem cells. The factor(s) which integrate with the ECM environment and responsible for stimulating stem cell self-renewal has not yet been identified. Discovery of such factors should be of great interest in gene therapy and bone marrow transplant applications

Briefly, polystyrene, non tissue culture treated, 96-well plates are coated with fn fragment at a coating concentration of 0.2 µg/ cm^2. Mouse bone marrow cells are plated (1,000 cells/well) in 0.2 ml of serum-free medium. Cells cultured in the presence of IL-3 (5 ng/ml) + SCF (50 ng/ml) would serve as the positive control, conditions under which little self-renewal but pronounced differentiation of the stem

cells is to be expected. Gene products of the invention (e.g., including, but not limited to, polynucleotides and polypeptides of the present invention, and supernatants produced in Example 31), are tested with appropriate negative controls in the presence and absence of SCF(5.0 ng/ml), where test factor supernates represent 10% of the total assay volume. The plated cells are then allowed to grow by incubating in a low oxygen environment (5% CO_2, 7% O_2, and 88% N_2) tissue culture incubator for 7 days. The number of proliferating cells within the wells is then quantitated by measuring thymidine incorporation into cellular DNA. Verification of the positive hits in the assay will require phenotypic characterization of the cells, which can be accomplished by scaling up of the culture system and using appropriate antibody reagents against cell surface antigens and FACScan.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

If a particular polypeptide of the present invention is found to be a stimulator of hematopoietic progenitors, polynucleotides and polypeptides corresponding to the gene encoding said polypeptide may be useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein. The gene product may also be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Additionally, the polynucleotides and/or polypeptides of the gene of interest and/or agonists and/or antagonists thereof, may also be employed to inhibit the proliferation and differentiation of hematopoietic cells and therefore may be employed to protect bone marrow stem cells from chemotherapeutic agents during chemotherapy. This antiproliferative effect may allow administration of higher doses of chemotherapeutic agents and, therefore, more effective chemotherapeutic treatment.

Moreover, polynucleotides and polypeptides corresponding to the gene of

interest may also be useful for the treatment and diagnosis of hematopoietic related disorders such as, for example, anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex-vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia.

Example 44: Human Dermal Fibroblast and Aortic Smooth Muscle Cell Proliferation

The polypeptide of interest is added to cultures of normal human dermal fibroblasts (NHDF) and human aortic smooth muscle cells (AoSMC) and two co-assays are performed with each sample. The first assay examines the effect of the polypeptide of interest on the proliferation of normal human dermal fibroblasts (NHDF) or aortic smooth muscle cells (AoSMC). Aberrant growth of fibroblasts or smooth muscle cells is a part of several pathological processes, including fibrosis, and restenosis. The second assay examines IL6 production by both NHDF and SMC. IL6 production is an indication of functional activation. Activated cells will have increased production of a number of cytokines and other factors, which can result in a proinflammatory or immunomodulatory outcome. Assays are run with and without co-TNFa stimulation, in order to check for costimulatory or inhibitory activity.

Briefly, on day 1, 96-well black plates are set up with 1000 cells/well (NHDF) or 2000 cells/well (AoSMC) in 100 µl culture media. NHDF culture media contains: Clonetics FB basal media, 1mg/ml hFGF, 5mg/ml insulin, 50mg/ml gentamycin, 2%FBS, while AoSMC culture media contains Clonetics SM basal media, 0.5 µg/ml hEGF, 5mg/ml insulin, 1µg/ml hFGF, 50mg/ml gentamycin, 50 µg/ml Amphotericin B, 5%FBS. After incubation at 37°C for at least 4-5 hours, culture media is aspirated and replaced with growth arrest media. Growth arrest media for NHDF contains fibroblast basal media, 50mg/ml gentamycin, 2% FBS, while growth arrest media for AoSMC contains SM basal media, 50mg/ml gentamycin, 50µg/ml Amphotericin B, 0.4% FBS. Incubate at 37°C until day 2.

On day 2, serial dilutions and templates of the polypeptide of interest are designed such that they always include media controls and known-protein controls. For both stimulation and inhibition experiments, proteins are diluted in growth arrest media. For inhibition experiments, TNFa is added to a final concentration of 2ng/ml (NHDF) or 5ng/ml (AoSMC). Add 1/3 vol media containing controls or polypeptides of the present invention and incubate at 37°C/5% CO_2 until day 5.

Transfer 60µl from each well to another labeled 96-well plate, cover with a plate-sealer, and store at 4°C until Day 6 (for IL6 ELISA). To the remaining 100 µl in the cell culture plate, aseptically add Alamar Blue in an amount equal to 10% of the culture volume (10µl). Return plates to incubator for 3 to 4 hours. Then measure fluorescence with excitation at 530nm and emission at 590nm using the CytoFluor. This yields the growth stimulation/inhibition data.

On day 5, the IL6 ELISA is performed by coating a 96 well plate with 50-100 ul/well of Anti-Human IL6 Monoclonal antibody diluted in PBS, pH 7.4, incubate ON at room temperature.

On day 6, empty the plates into the sink and blot on paper towels. Prepare Assay Buffer containing PBS with 4% BSA. Block the plates with 200 µl/well of Pierce Super Block blocking buffer in PBS for 1-2 hr and then wash plates with wash buffer (PBS, 0.05% Tween-20). Blot plates on paper towels. Then add 50 µl/well of diluted Anti-Human IL-6 Monoclonal, Biotin-labeled antibody at 0.50 mg/ml. Make dilutions of IL-6 stock in media (30, 10, 3, 1, 0.3, 0 ng/ml). Add duplicate samples to top row of plate. Cover the plates and incubate for 2 hours at RT on shaker. Plates are washed with wash buffer and blotted on paper towels. Dilute EU-labeled Streptavidin 1:1000 in Assay buffer, and add 100 µl/well. Cover the plate and incubate 1 h at RT. Plates are again washed with wash buffer and blotted on paper towels. Add 100 µl/well of Enhancement Solution and shake for 5 minutes. Read the plate on the Wallac DELFIA Fluorometer. Readings from triplicate samples in each assay are tabulated and averaged.

A positive result in this assay suggests AoSMC cell proliferation and that the polypeptide of the present invention may be involved in dermal fibroblast

proliferation and/or smooth muscle cell proliferation. A positive result also suggests many potential uses of polypeptides, polynucleotides, agonists and/or antagonists of the polynucleotide/polypeptide of the present invention which gives a positive result. For example, inflammation and immune responses, wound healing, and angiogenesis, as detailed throughout this specification. Particularly, polypeptides of the present invention and polynucleotides of the present invention may be used in wound healing and dermal regeneration, as well as the promotion of vasculargenesis, both of the blood vessels and lymphatics. The growth of vessels can be used in the treatment of, for example, cardiovascular diseases. Additionally, antagonists of polypeptides and polynucleotides of the invention may be useful in treating diseases, disorders, and/or conditions which involve angiogenesis by acting as an anti-vascular (e.g., anti-angiogenesis). These diseases, disorders, and/or conditions are known in the art and/or are described herein, such as, for example, malignancies, solid tumors, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; artheroscleric plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uvietis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis. Moreover, antagonists of polypeptides and polynucleotides of the invention may be useful in treating anti-hyperproliferative diseases and/or anti-inflammatory known in the art and/or described herein.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

Example 45: Cellular Adhesion Molecule (CAM) Expression on Endothelial Cells

The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

Briefly, endothelial cells (e.g., Human Umbilical Vein Endothelial cells (HUVECs)) are grown in a standard 96 well plate to confluence, growth medium is removed from the cells and replaced with 100 µl of 199 Medium (10% fetal bovine serum (FBS)). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 µl volumes). Plates are then incubated at 37°C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 µl of 0.1% paraformaldehyde-PBS(with Ca++ and Mg++) is added to each well. Plates are held at 4°C for 30 min. Fixative is removed from the wells and wells are washed 1X with PBS(+Ca,Mg) + 0.5% BSA and drained. 10 µl of diluted primary antibody is added to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 µg/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed three times with PBS(+Ca,Mg) + 0.5% BSA. 20 µl of diluted ExtrAvidin-Alkaline Phosphotase (1:5,000 dilution, refered to herein as the working dilution) are added to

each well and incubated at 37°C for 30 min. Wells are washed three times with PBS(+Ca,Mg)+0.5% BSA. Dissolve 1 tablet of p-Nitrophenol Phosphate pNPP per 5 ml of glycine buffer (pH 10.4). 100 µl of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphotase in glycine buffer: 1:5,000 (10^0) > $10^{-0.5}$ > 10^{-1} > $10^{-1.5}$. 5 µl of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 µl of pNNP reagent is then added to each of the standard wells. The plate is incubated at 37°C for 4h. A volume of 50 µl of 3M NaOH is added to all wells. The plate is read on a plate reader at 405 nm using the background subtraction option on blank wells filled with glycine buffer only. Additionally, the template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

Example 46: Alamar Blue Endothelial Cells Proliferation Assay

This assay may be used to quantitatively determine protein mediated inhibition of bFGF-induced proliferation of Bovine Lymphatic Endothelial Cells (LECs), Bovine Aortic Endothelial Cells (BAECs) or Human Microvascular Uterine Myometrial Cells (UTMECs). This assay incorporates a fluorometric growth indicator based on detection of metabolic activity. A standard Alamar Blue Proliferation Assay is prepared in EGM-2MV with 10 ng /ml of bFGF added as a source of endothelial cell stimulation. This assay may be used with a variety of endothelial cells with slight changes in growth medium and cell concentration. Dilutions of the protein batches to be tested are diluted as appropriate. Serum-free medium (GIBCO SFM) without bFGF is used as a non-stimulated control and Angiostatin or TSP-1 are included as a known inhibitory controls.

Briefly, LEC, BAECs or UTMECs are seeded in growth media at a density of 5000 to 2000 cells/well in a 96 well plate and placed at 37-C overnight. After the overnight incubation of the cells, the growth media is removed and replaced with

GIBCO EC-SFM. The cells are treated with the appropriate dilutions of the protein of interest or control protein sample(s) (prepared in SFM) in triplicate wells with additional bFGF to a concentration of 10 ng/ ml. Once the cells have been treated with the samples, the plate(s) is/are placed back in the 37° C incubator for three days. After three days 10 ml of stock alamar blue (Biosource Cat# DAL1100) is added to each well and the plate(s) is/are placed back in the 37°C incubator for four hours. The plate(s) are then read at 530nm excitation and 590nm emission using the CytoFluor fluorescence reader. Direct output is recorded in relative fluorescence units.

Alamar blue is an oxidation-reduction indicator that both fluoresces and changes color in response to chemical reduction of growth medium resulting from cell growth. As cells grow in culture, innate metabolic activity results in a chemical reduction of the immediate surrounding environment. Reduction related to growth causes the indicator to change from oxidized (non-fluorescent blue) form to reduced (fluorescent red) form. i.e. stimulated proliferation will produce a stronger signal and inhibited proliferation will produce a weaker signal and the total signal is proportional to the total number of cells as well as their metabolic activity. The background level of activity is observed with the starvation medium alone. This is compared to the output observed from the positive control samples (bFGF in growth medium) and protein dilutions.

Example 47: Detection of Inhibition of a Mixed Lymphocyte Reaction

This assay can be used to detect and evaluate inhibition of a Mixed Lymphocyte Reaction (MLR) by gene products (e.g., isolated polypeptides). Inhibition of a MLR may be due to a direct effect on cell proliferation and viability, modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, or modulation of cytokine production by accessory cells. Multiple cells may be targeted by these polypeptides since the peripheral blood mononuclear fraction used in this assay includes T, B and

natural killer lymphocytes, as well as monocytes and dendritic cells.

Polypeptides of interest found to inhibit the MLR may find application in diseases associated with lymphocyte and monocyte activation or proliferation. These include, but are not limited to, diseases such as asthma, arthritis, diabetes, inflammatory skin conditions, psoriasis, eczema, systemic lupus erythematosus, multiple sclerosis, glomerulonephritis, inflammatory bowel disease, crohn's disease, ulcerative colitis, arteriosclerosis, cirrhosis, graft vs. host disease, host vs. graft disease, hepatitis, leukemia and lymphoma.

Briefly, PBMCs from human donors are purified by density gradient centrifugation using Lymphocyte Separation Medium (LSM®, density 1.0770 g/ml, Organon Teknika Corporation, West Chester, PA). PBMCs from two donors are adjusted to 2 x 10^6 cells/ml in RPMI-1640 (Life Technologies, Grand Island, NY) supplemented with 10% FCS and 2 mM glutamine. PBMCs from a third donor is adjusted to 2 x 10^5 cells/ml. Fifty microliters of PBMCs from each donor is added to wells of a 96-well round bottom microtiter plate. Dilutions of test materials (50 μl) is added in triplicate to microtiter wells. Test samples (of the protein of interest) are added for final dilution of 1:4; rhuIL-2 (R&D Systems, Minneapolis, MN, catalog number 202-IL) is added to a final concentration of 1 μg/ml; anti-CD4 mAb (R&D Systems, clone 34930.11, catalog number MAB379) is added to a final concentration of 10 μg/ml. Cells are cultured for 7-8 days at 37°C in 5% CO_2, and 1 μC of [^{3}H] thymidine is added to wells for the last 16 hrs of culture. Cells are harvested and thymidine incorporation determined using a Packard TopCount. Data is expressed as the mean and standard deviation of triplicate determinations.

Samples of the protein of interest are screened in separate experiments and compared to the negative control treatment, anti-CD4 mAb, which inhibits proliferation of lymphocytes and the positive control treatment, IL-2 (either as recombinant material or supernatant), which enhances proliferation of lymphocytes.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both incorporated herein by reference in their entireties. Moreover, the hard copy of and the corresponding computer readable form of the Sequence Listing of Serial No. 60/124,270 are also incorporated herein by reference in their entireties.

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Applicant's or agent's file reference number	PA103PCT	International applicati. .o.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution: American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209059

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

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ATCC Deposit No. 209059

CANADA

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NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

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Page 2
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DENMARK

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application

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Name of depositary institution: American Type Culture Collection

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209060

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CANADA

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UNITED KINGDOM

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Page 2
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Applicant's or agent's file reference number	?A103PCT	International application N

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Date of deposit	Accession Number
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Name of depositary institution
American Type Culture Collection

Address of depositary institution *(including postal code and country)*
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209062

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Page 2
ATCC Deposit No. 209062

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application i

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution: American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209063

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application RO/US MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. 209063

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

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Page 2
ATCC Deposit No. 209063

DENMARK

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International applicatior

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

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B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution: American Type Culture Collection

Address of depositary institution *(including postal code and country)*
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209064

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

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☑ This sheet was received with the international application RO/US 08 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3678	Authorized officer

ATCC Deposit No. 209064

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 209064

DENMARK

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SWEDEN

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NETHERLANDS

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429

Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution: American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209065

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

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☑ This sheet was received with the international application RO/US 03 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3870	Authorized officer

Form PCT/RO/134 (July 1992)

ATCC Deposit No. 209065

CANADA

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NORWAY

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 209065

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SWEDEN

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Applicant's or agent's file reference number	PA103PCT	International application No.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution
American Type Culture Collection

Address of depositary institution *(including postal code and country)*
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209066

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

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RO/US 03 MAR 2000	
Authorized officer: Yolanda Harrod, PCT/Internat'l Appl Processing Div., (703) 305-3670	Authorized officer

ATCC Deposit No. 209066

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 209066

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Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209067

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

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Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. 209067

CANADA

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UNITED KINGDOM

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Page 2
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Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution
American Type Culture Collection

Address of depositary institution *(including postal code and country)*
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209068

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

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Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. 209068

CANADA

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UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 209068

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution
American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
20 May 1997	209069

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application RO/US 03 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3870	Authorized officer

ATCC Deposit No. 209069

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

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Page 2
ATCC Deposit No. 209069

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution
American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
12 January 1998	209579

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application 02 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 209579

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 209579

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
12 January 1998	209578

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

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Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. 209578

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 209578

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72 , line N/A .

B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
16 July 1998	203067

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application RO/US 03 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Harrod PCT/Internat'l Appl Processing Div. (703) 305-3679	Authorized officer

ATCC Deposit No. 203067

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 203067

DENMARK

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution
American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
16 July 1998	203068

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application RO/US 08 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3679	Authorized officer

ATCC Deposit No. 203068

CANADA

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NORWAY

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 203068

DENMARK

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Applicant's or agent's file reference number	PA103PCT	International application No.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
1 February 1999	203609

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application RO/US 03 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3673	Authorized officer

ATCC Deposit No. 203609

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 203609

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PA103PCT	International application No.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
1 February 1999	203610

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application RO/US 08 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

Form PCT/RO/134 (July 1992)

ATCC Deposit No. 203610

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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FINLAND

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 203610

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SWEDEN

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NETHERLANDS

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462

Applicant's or agent's file reference number	PA103PCT	International application No.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
17 November 1998	203485

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

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Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. 203485

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 203485

DENMARK

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application No.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
18 June 1999	PTA-252

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

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Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. PTA-252

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

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UNITED KINGDOM

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Page 2
ATCC Deposit No. PTA-252

DENMARK

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application No

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet ☐

Name of depositary institution
American Type Culture Collection

Address of depositary institution *(including postal code and country)*
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
18 June 1999	PTA-253

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

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Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. PTA-253

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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UNITED KINGDOM

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Page 2
ATCC Deposit No. PTA-253

DENMARK

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA103PCT	International application No.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 72, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution

American Type Culture Collection

Address of depositary institution *(including postal code and country)*

10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
22 December 1999	PTA-1081

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application RO/US 03 MAR 2000	☐ This sheet was received by the International Bureau on:
Authorized officer Yolanda Harrod PCT/Internat'l Appl Processing Div. (703) 305-3670	Authorized officer

ATCC Deposit No. PTA-1081

CANADA

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NORWAY

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UNITED KINGDOM

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Page 2
ATCC Deposit No. PTA-1081

DENMARK

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What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;

(c) a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO:X or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;

(d) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;

(e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;

(f) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X, having biological activity;

(g) a polynucleotide which is a variant of SEQ ID NO:X;

(h) a polynucleotide which is an allelic variant of SEQ ID NO:X;

(i) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;

(j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide

sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;

(b) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone, having biological activity;

(c) a polypeptide domain of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;

(d) a polypeptide epitope of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;

(e) a full length protein of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;

(f) a variant of SEQ ID NO:Y;

(g) an allelic variant of SEQ ID NO:Y; or

(h) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

22. A method of identifying an activity in a biological assay, wherein the method comprises:

(a) expressing SEQ ID NO:X in a cell;

(b) isolating the supernatant;

(c) detecting an activity in a biological assay; and

(d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

SEQUENCE LISTING

<110> Craig Rosen,
Steve Ruben

<120> Human Breast and Ovarian Cancer Associated Gene Sequences and Polypeptides

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<211> 2438
<212> DNA
<213> Homo sapiens

<220>
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<222> (117)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (681)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (713)
<223> n equals a,t,g, or c

<220>
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<222> (2413)
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<210> 14
<211> 2347
<212> DNA
<213> Homo sapiens

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gaaaaaa 2347

<210> 15
<211> 2006
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (862)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1006)
<223> n equals a,t,g, or c

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<210> 16
<211> 986
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (613)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (932)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (933)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (985)
<223> n equals a,t,g, or c

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<210> 17
<211> 1589
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (25)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (555)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (809)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1033)
<223> n equals a,t,g, or c

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ccatgattcg cccaaagcca gacagcaacg gggaggccra gtgcaggctg gcaccgcctt 240
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<210> 18
<211> 846
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (746)
<223> n equals a,t,g, or c

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<211> 2192
<212> DNA
<213> Homo sapiens

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<222> (115)
<223> n equals a,t,g, or c

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<220>
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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2143)
<223> n equals a,t,g, or c

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<210> 20
<211> 1011
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (54)
<223> n equals a,t,g, or c

<400> 20

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gacagtttta ccgcattccr tccactcccg attccttcat ggatccggcg tctgcacttt 180
acagaggtcc aatcacgcgg acccagaacc ccatggtgac cgggacctca gtcctcggcg 240
ttaagttcga gggcggagtg gtgattgccg cagacatgct gggatcctac ggctccttgg 300
ctcgtttccg caacatctct cgcattatgc gagtcaacaa cagtaccatg ctgggtgcct 360
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ccccttcgct ggccactggt tatggtgcat acttggctca gcctctgctg cgagaagttc 660
tggagaagca gccagtgcta agccagaccg aggcccgcga cttagtagaa cgctgcatgc 720
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taactttgaa cttggctagt tcaaagatag actcttcttt tgtaaagtaa ataaattctt 960
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<210> 21
<211> 2019
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2003)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2007)
<223> n equals a,t,g, or c

<400> 21
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<210> 22
<211> 2022
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1588)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1615)
<223> n equals a,t,g, or c

<400> 22
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tgtgacgcca ctcaccttta ctgaggtgca cgagggccgt gctgacatca tgatcgactt 180
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gctacccact gagtctcagc ccagatgact gcaggggcgt tcaacaccta tatggccagc 480
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<210> 23
<211> 1126
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1126)

<223> n equals a,t,g, or c

<400> 23
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gtaaacgtgt gacgggggaa agccaaggtc tggagaagct cccaggaaca ayygatggcc 180
ttgcagcact cacacaggac ccccttcccc taccccctcc tctctgccgc aatacaggaa 240
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<210> 24
<211> 2598
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2304)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2500)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2533)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2553)
<223> n equals a,t,g, or c

<400> 24
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<210> 25
<211> 411
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (358)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (368)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (381)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (387)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (392)
<223> n equals a,t,g, or c

<400> 25
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ctctgagctc caggtcacaa tgcacgacac ccggggccgc agtcccccat accagctngg 360
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<210> 26
<211> 657
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (634)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (652)
<223> n equals a,t,g, or c

<400> 26
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cagcccctct tcccttcctc cattgcacat gaacatatgt ccatccatat atattcatca 180
gaatgttaat ttattttgct ccctctgtta ggtccatttt ctaagggtag aagaggcaag 240

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tctgcacgtt gctgaaggtc caggcttgcc tcaagttcca tgcttgagca ataaagtgga 600
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<210> 27
<211> 1903
<212> DNA
<213> Homo sapiens

<400> 27

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ggaagggtac tacaaggaca agctctttga ccagcgggag ctccgctttg agattggcga 420
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acaacctgtc cagatgaggc cactgttatc ccagtctgtg aggggcgatc acagcccagg 1860
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<210> 28
<211> 1333
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1311)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1313)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1319)
<223> n equals a,t,g, or c

<400> 28
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aaaaaaaaaa ttt                                                     1333
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<210> 29
<211> 1327
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (573)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1307)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1325)
<223> n equals a,t,g, or c

<400> 29
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agcagcgcga gcagatggag cagatgaagc agcgcatcgs ggaggagaac atcatgaaat 180
ccaacattga caagaagttc tctgcgcact acgacgcggt ggaggcagag ctcaagtcca 240
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cgtgtcctgc ccctgccaca tcagtgactg ctttattctt ttccaataaa gaagtgcacg 1260
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agggngg 1327

<210> 30
<211> 709
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (696)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (701)
<223> n equals a,t,g, or c

<400> 30

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aatcctagaa aactcacaaa atgtgtgatg cttttgtagg tacctggaaa cttgtctcca 120
gtgaaaactt tgatgattat atgaaagaag taggagtggg ctttgccacc aggaaagtgg 180
ctggcatggc caaacctaac atgatcatca gtgtgaatgg ggatgtgatc accattaaat 240
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cactgcagat gacaggaaag tcaagagcac cataacctta gatgggggtg tcctggtaca 360
tgtgcagaaa tgggatggaa aatcaaccac cataaagaga aaacgagagg atgataaact 420
ggtggtggaa tgcgtcatga aaggcgtcac ttccacgaga gtttatgaga gagcataagc 480
caagggacgt tgacctggac tgaagttcgc attgaactct acaacattct gtgggatata 540
ttgttcaaaa agatattgtt gttttccatg atttagcaag caactaattt tctcccaagc 600
tgattttatt caatatggtt acgttggtta aataaacttt ttttagattt aaaaaaaaaa 660
aaaaaaaacc ycgggggggg gcccggtacc caattngccc nttaggggg 709

<210> 31
<211> 1108
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (389)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (397)
<223> n equals a,t,g, or c

<400> 31
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ccaaacaact tttaattgat ccagaagatg atgtaagaga taatatttta aaatatgatg 120
aagaaggtgg aggagaagaa gaccaggact atgacttgag ccagctgcag cagcctgaca 180
ctgtggagcc tgatgccatc aagcctgtgg gaatcygacg aatggatgaa agacccatcc 240
acgccgagcc ccagtatccg gtccgatctg cagccccaca ccctggagac attggggact 300
tcattaatga gggccttaaa gcggctgaca atgaccccac agctccacca tatgactccc 360
tgttagtgtt tgactatgaa ggcagtggnt ccactgntgg gtccttgagc tcccttaatt 420
cctcaagtag tggtggtgag caggactatg attacctgaa cgactggggg ccacggttca 480
agaaacttgc tgacatgtat ggtggaggtg atgactgaac ttcagggtga acttggtttt 540
tggacaagta caaacaattt caactgatat tcccaaaaag cattcagaag ctaggcttta 600
actttgtagt ctactagcac agtgcttgct ggaggctttg gcataggctg caaaccaatt 660
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cttgaatttt acagtacaga agcactggga ttttatgtgc ctttttgtac ctttttcaga 780
ttggaattag ttttctgttt aaggctttaa tggtactgat ttctgaaacg ataagtaaaa 840
gacaaaatat tttgtggtgg gagcagtaag ttaaaccatg atatgcttca acacgctttt 900
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<210> 32
<211> 526

<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (502)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (524)
<223> n equals a,t,g, or c

<400> 32
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tacacattta acacacagta gcaaattttg aacgatgtga ttgatataac ctaacaaatc 120
tgagccagtt attattagag ttgcagaata gaaacttgaa gtgctaaatg gaataatcca 180
aaggaaattt tttaaatgca ggttctagct gaaaaattca actataagaa aattgtattt 240
atataacatt tactattttt gaagactagt gagatttctg taataatttt aattctttaa 300
aaagtgaaag cttgttgtaa agatattttc tttttgttat tagaaggaaa tacaaagaga 360
aaaatttctt tctttcatgg ggcatttgat aatttcagtc tttgacgatt tgtaagccta 420
gaatatacta agctgaataa cagctctttg gcctcagaat tttccagtag ccagtawttc 480
yggattaact aagttggaaa cncytattag gaacctccag tggnga 526

<210> 33
<211> 555
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (494)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (521)
<223> n equals a,t,g, or c

<400> 33
ccggaccctg cacccagcga ctgggccccg cgcgcgccct ccgcgagggt ggaggcggcg 60
gctgtgtgcg cagggcccgg caccggactg ggaccctggc gtccctccag gccttgcctc 120
ctgcgggags acagtttggc ttcacttctc tgaccccagc ctcggccgta aagtgaaaga 180
gaccggacca gcttcagctt tcggactctg gttcttggat cgtgtcctct ccccctcgcc 240
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ttgctgggcc tcccacctca aggaggggaa ggttgtacag cccgaacccg tggagcaatg 420
ccctgtctgg cctccaaaac caaaataaaa ctgggtcact ttacaaaaaa aaaaaaaaaa 480
aagggcccgg gaanaccgga ccggtacctg caggcgtacc ngtttcccta tagtgagttg 540
tattagcgtt gcata 555

<210> 34
<211> 347
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (288)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (328)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (335)
<223> n equals a,t,g, or c

<400> 34
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gggggtggag gcggctcctg cratctaaag ggacttgaga ctctcaccgg ccgcgcgcca 120
tgagggccct gtgggtgctg ggcctctcct gcrtcctgct gaccttcggg tcggtccgar 180
ctgaygatga agtcgatgtg gatggtacag tggaagagga tctgggtaaa agtagagaag 240
gttcaaggac agatgatgaa gtagtacaga gagaggaaga agctattnca gttggatgga 300
ttaaatgcat cccaaataag agaacttnag agagnaagtc cagaaaa 347

<210> 35
<211> 750
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (701)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (731)
<223> n equals a,t,g, or c

<400> 35
gggtggcttc cttgtggttc ctcagtggtg cctgcaaccc ctggttcacc tccttccagg 60
ttctggctcc ttccagccat ggctctcaga gtccttctgt taacagcctt gaccttatgt 120
catgggttca acttggacac tgaaaacgca atgaccttcc aagagaacgc aaggggcttc 180
gggcagagcg tggtccagct tcagggatcc agggtggtgg ttggagcccc ccaggagata 240
gtggctgcca accaaagggg cagcctctac cagtgcgact acagcacagg ctcatgcgag 300
cccatccacc tgcaggtccc cgtggaggcc gtgaacatgt ccctgggcct gtccctggca 360
gccaccacca gcccccctca gctgctggcc tgtggtccca ccgtgcacca gacttgcagt 420

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gagaacacgt atgtgaaagg gctctgcttc ctgtttggat ccaacctacg gcagcagccc 480
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gaattccgga ttcactttac ttcaaagagt tccagaacaa ncctaaccca agatcactgg 720
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<210> 36
<211> 1291
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (29)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (298)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (695)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (795)
<223> n equals a,t,g, or c

<400> 36
aagaaaaatg tactacgcct gtcctgtang aagctgaaga tttttgcaat gcccatgcag 60
gatatcaaga tgatcctgaa aatggtgcag ctggactcta ttgaagattt gggaagtgac 120
ttgtacctgg aagctaccca ccttggcgaa attttctcct tacctgggcc agatgattaa 180
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gaacccсttg gaaaccctct caataactaa ctgccggctt tcggaagggg atgtgatgca 420
tctgtcccag agtcccagcg tcagtcagct aagtgtcctg agtctaagtg gggtcatgct 480
gaccgatgta agtcccgagc cctccaagc tctgctggag agagcctctg ccaccctcca 540
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atgttcagtg aggaaaaaaa ggggagttgg ggataggcag atgttgactt grggagktaa 1140
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agawtctggc ttgggaagta catgtaggag ttaatccctg tgtagactgt tgtaaagaaa 1260
ctgttgaaaa taaagagaag caatgtgaag c 1291

<210> 37
<211> 1535
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1413)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1526)
<223> n equals a,t,g, or c

<400> 37
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agtacgctgg gctggaccac gagctggcct tctctcgtct gatcgtggag ctgcggcggc 120
tgcacccagg ccacgtgctg cccgacgagg agctgcagtg ggtgttcgtg aatgcgggtg 180
gctggatggg cgccatgtgc cttctgcacg cctcgctgtc cgagtatgtg ctgctcttcg 240
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ctgctgcatt ctctgtccat ctgtctgttt ctattaataa agatttgttg atctgttcca 1500
aaaaaaaaaa aaaaaaaaaa aaaaanggggg gggct 1535

<210> 38
<211> 295
<212> DNA

<213> Homo sapiens

<400> 38
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acacccgata gcgaaagtta tcgggtgttt tcttgaacat cgacggcgaa ggtaacccca 180
ttaatcacca gtcaaaactt ttcaccagcg tcactcgcca gcattacgca tcggtacaat 240
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<210> 39
<211> 1300
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (641)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1297)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1298)
<223> n equals a,t,g, or c

<400> 39
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ccccggtatc agcgcttcct cattctttga atccgcggct ccgcggtctt cggcgtcaga 180
ccagccggag gaagcctgtt tgcaatttaa gcgggctgtg aacgcccagg gccggcgggg 240
gcggggccga ggcgggccat tttraataaa gaggcgtgcc ttccaggcag gctctataag 300
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gcggctgcta cgaggcggtg tgctgcctgt cggaacgcag tctggccatc gcccggggcc 480
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<210> 40
<211> 215
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (210)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (213)
<223> n equals a,t,g, or c

<400> 40
cagaaacaga agttcacact aacagagtat ggttttaatt ttcctttgaa tgaaaaggat 60
agaaagataa aattgtgtat tgttaacatg taaataaaat tggagctaat ttgaaactag 120
cttctcaata acttcatctt tctagagact cattacctgt gggcttgtcm aacctggact 180
atttggccaa atwggttgga taaaaaaggn atntt 215

<210> 41
<211> 474
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (85)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (216)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (374)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (449)
<223> n equals a,t,g, or c

<400> 41
tcgacccacg cgtccgggag actacggtaa aggcgcgcgc acgcagccaa catgccggtg 60
gcccggagct gggtttgtcg caagnctacg tgacccctcg gaggcccttt gagaagtcgc 120

ggctcgacca agagctgaag ctgataggcg agtacgggct ccggaacaaa cgtgaggtgt 180
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acgagaagga cccgcggcgc ctgtttgagg gcaatgcctt gcttcggcga ctggtgcgca 300
ttggagtgct ggacgagggc aagatgaagc tggattatat cctgggtctg aagatgagga 360
ttcttggaga grcntctgca gacccaggty tttcaagctg ggttggcca atccatccac 420
catgccctgt gctgatccgc caggccacnc aggtccgaaa gcaagtggtg aaca 474

<210> 42
<211> 425
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (375)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (403)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (418)
<223> n equals a,t,g, or c

<400> 42
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tcgtcttatg ggactggagc tctcaagtct catatcatgg cggcaaaggc tgtagcaaat 120
accatgagaa catcacttgg accaaatgga cttgataaaa tgatggtgga caaggacggc 180
gacgtgacgg tcacaaacga cggtgccacg attctgagca tgatggatgt cgatcaccag 240
attgccaagc tgatggtgga gctgtccaaa tcccaggatg atgaaatcgg agatggggac 300
cacgggggtg gttgtcctgg ccggcgccct gctggaagga ggccgagcag ctgctggacc 360
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gagca 425

<210> 43
<211> 1187
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (33)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (41)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1149)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1156)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1160)
<223> n equals a,t,g, or c

<400> 43
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aagaccatca ccctcgaggt tgagcccagt gacaccatcg agaatgtcaa ggcaaagatc 180
caagataagg aaggcatccc tcctgaccag cagaggctga tctttgctgg aaaacagctg 240
gaagatggkc gcaccctgtc tgactacaac atccagaaag agtccaccyt gcacctggtr 300
ctccgtctca gaggtgggat gcaaatcttc gtgaagacac tcactggcaa gaccatcacc 360
cttgaggtcg agcccagtga cacyatcgag aacgtcaaag caaagatcca rgacaaggaa 420
ggcattcctc ctgaccagca gaggttgatc tttgccggaa agcagctgga agatgggcgc 480
accctgtctg actacaacat ccagaaagag tctaccctgc acctggtgct ccgtctcaga 540
ggtgggatgc agatcttcgt gaagaccctg actggtaaga ccatcacyct cgargtggag 600
ccgagtgaca ccattgagaa tgtcaaggca aagatccaag acaaggaagg catccctcct 660
gaccagcaga ggttgatctt tgctgggaaa cagctggaag atggacgcac cctgtctgac 720
tacaacatcc agaaagagtc caccctgcac ctggtgctcc gtcttagagg tgggatgcag 780
atcttcgtga agaccctgac tggtaagacc atcactctcg aagtggagcc gagtgacacc 840
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accctgactg gtaagaccat cacyctcgaa gtggagccga gtgacaccat ygagaatgtc 1080
aaggcaagat ccagacaagg aaggcatcct cctgaccagc agargttgat tttgctggga 1140
aaarcttgna aatggncgan cccttttgat taaaatcccg aaagttc 1187
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<210> 44
<211> 515
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (217)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (465)

<223> n equals a,t,g, or c

<400> 44
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accggtctac ctcgctagca tgtcgggccg cggcaagact ggcggcaagg cccgcgccaa 120
ggccaagtcg cgctcgtcgc gcgccggcct ccagttccca gtgggccgtg tacaccggct 180
gctgcggaag ggccactacg ccgagcgcgt tggcgcnggc rcgccagtgt acctggcggc 240
agtgctggag tacctcaccg ctgagatcct ggagctggcg ggcaatgcgg cccgcgacaa 300
caagaagacg cgaatcatcc cccgccacct gcagctggcc atccgcaacg acgaggagct 360
caacaagctg ctgggcggcg tgacgatcgc ccagggaagg cgtyctgccc aacatccagg 420
ccgtgsttgy tgcccaagaa gaccagcgcc accgtggggc cgaangccct tcgggggca 480
agaaagggca accaaggctt cccaaggagt actaa 515

<210> 45
<211> 1499
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1476)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1492)
<223> n equals a,t,g, or c

<400> 45
gcgagtgcgc gctcctcctc gcccgccgct aggtccatcc cggcccagcc accatgtcca 60
tccacttcag ctcccccggca tccgcgaggt caccattaac cagagcctgc tggccccgct 120
gcggctggac gccgacccct ccctccagcg ggtgcgccag gaggagagcg agcagatcaa 180
gaccctcaac aacaagtttg cctccttcat cgacaaggtg cggtttctgg agcagcagaa 240
caagctgctg gagaccaagt ggacgctgct gcaggagcag aagtcggcca agagcagccg 300
cctcccagac atctttgagg cccagattgc tggccttcgg ggtcagcttg aggcactgca 360
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caagaataag tacgaagatg aaattaaccg ccgcacagct gctgagaatg agtttgtggt 480
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cactcctcca gccaccaccc acaatcacaa gaagattccc acccctgcct cccatgcctg 1380
gtcccaagac agtgagacag tctggaaagt gatgtcagaa tagcttccaa taaagcagcs 1440
tcattctgag gcctgagtga aaaaaaaaaa aaaaanaaaa aaaaaaattt tngggggg 1499

<210> 46
<211> 393
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (167)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (178)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (219)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (359)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (372)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (378)
<223> n equals a,t,g, or c

<400> 46
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gaagatgttc tcgtccgtgg cgcatctggc cgggcgaacc ccttcaacgc gccccacctg 120
cagctggtac acgatggcct cacgggcacc gaagcagccc cgtgggnacc cccgggcncg 180
ccccgaacgt tcccgcaatc tggcagcagc cgctgtggna agagtacagt tgcgaatatg 240
gctccatgaa gttttatgca ctgtgtggct ttggtggggt cttaagttgt ggtctgacac 300
acactgctgt cgttcctctg gatttagtga aatgccgaat gcargtggac ccccagaant 360
acaagggcak wnttaatngg attctcatta aca 393

<210> 47
<211> 238
<212> DNA

<213> Homo sapiens

<400> 47
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cgcggccgga ccggttcaac ttctcatctt tgttcttctt catatactat aggctgtttg 180
ctgtggttta gtcaaaaagc catgtagaat gcctgccttt tgaagaccac ttttaagg 238

<210> 48
<211> 939
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (937)
<223> n equals a,t,g, or c

<400> 48
gccaccatct tggaacggga ggcggagcag agtcgactgg gagcgaccga gcgggccgcc 60
gccgccgcca tgaaccccga atatgactac ctgtttaagc tgcttttgat tggcgactca 120
ggcgtgggca agtcatgcct gctcctgcgg tttgctgatg acacgtacac agagagctac 180
atcagcacca tcggggtgga cttcaagatc cgaaccatcg agctggatgg caaaactatc 240
aaacttcaga tctgggacac agcgggccag gaacggttcc ggaccatcac ttccagctac 300
taccgggggg ctcatggcat catcgtggtg tatgacgtca ctgaccagga atcctacgcc 360
aacgtgaagc agtggctgca ggagattgac cgctatgcca gcgagaacgt caataagctc 420
ctggtgggca acaagagcga cctcaccacc aagaaggtgg tggacaacac cacagccaag 480
gagtttgcag actctctggg catccccttc ttggagacga gcgccaagaa tgccaccaat 540
gtcgagcagg cgttcatgac catggctgct gaaatcaaaa agcggatggg gcctggagca 600
gcctctgggg gcgagcggcc caatctcaag atcgacagca cccctgtaaa gccggctggc 660
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gctgcttgtg ctgttgcctc taagtgaatt tccaaangc 939

<210> 49
<211> 1771
<212> DNA
<213> Homo sapiens

<400> 49
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aaccagggtc tcatccgcat gtataaggcc gagtgcctgg agaagttccc tgtgatccag 180
cacttcaagt tcgggagcct gctgcccatc catcctgtca cgtcgggcta ggaggggcca 240
agccgaagag ccacccaggc cacagttcct gtgcctgcct tccccacccc agcagtggcc 300
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tggcgagatg ggcttgaggg ggctcagagc ataaggcttc agggcccaag ttgggagaag 420
tgaccaaagt gtagccagtt ttctgagttc ccgtgtgcta gactggccag aagagagggt 480
ctggggcctg gtcactcggc cactctctcc tgtttctggc ctcttctccc ttcactcccg 540

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cacccccttcc tggctccccc atccccctat ggctcccagc cccttgcacc ctcattgctg 1680
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<210> 50
<211> 397
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (201)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (207)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (352)
<223> n equals a,t,g, or c

<400> 50
gggtcgaccc acgcgtccgc tcgctccggg atcgcccgcg ctagagacgc atagcgctct 60
aatcgctcgc acgcaccggc cctcgctcgc tcgcccgtcc gtgccgccgc cgcccagccc 120
accgccaccc tttgcagcca tgtccaccag gtcygtgtcc tcgtcytcct accgcagatg 180
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ccgcacctac agcctgggca gcgcctgcgc cccagcacca gccgcagcct ctamamctcg 300
tccccgggcg gcgcgtatgt tcacggctcc ttccgcggtg cgcctgcgga anatgttgcc 360
ccggcgttgc gcttgctggc aggattccgt ggaattt 397

<210> 51
<211> 1635
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1422)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1617)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1620)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1629)
<223> n equals a,t,g, or c

<400> 51
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tgcctgatga caataaagct tgttgactca gctaaaaaaa aaaaaaaaaa aaaaaaaaaa 1560
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaanttn 1620
gggggggggnc ccccc 1635

<210> 52
<211> 1780
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1780)
<223> n equals a,t,g, or c

<400> 52
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ggggtgatcc tgctggctgt tggagtctgg ggcaaactta ctctgggcac ctatatctcc 180
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aatttaaaaa tgagtgtgaa gggggaacaa gtcaaaatat ttttaaaaga tcttcaaaaa 1680
taatgcctct gtctagcatg ccaacaagaa tgcattgata ttgtgaacat ttgtgatata 1740
tgtattaata aatagagcaa ttacaagcaa aaaaaaatgn 1780

<210> 53
<211> 490
<212> DNA
<213> Homo sapiens

<400> 53
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aggcaggaga atacccctcc ctaagccctt agtgtgtgcc gagcttgctt tgtgatgttg 180
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<210> 54
<211> 1944
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (466)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (634)
<223> n equals a,t,g, or c

<220>
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<222> (1308)
<223> n equals a,t,g, or c

<400> 54
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gagaccagat gggtttgccc cagg 1944

<210> 55
<211> 994
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (896)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (971)
<223> n equals a,t,g, or c

<400> 55
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atcatggcca tccgccggaa ccgcgtggcc ctgaagggca acatcgaaac caaccataac 480
ctgccaccgt cgcacaaatc tcgaaacaac atccttcgca ccagcctgga cctctatgcc 540
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gccttcaagc tggcgcagga gagcgggcgc aagaaagtga cggccgtgca caaggccaac 780
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cctcagwtca ccttcgagaa catgattgtg gataacacca ccatgcagct ggtgtnccgg 900
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<210> 56
<211> 328

<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (123)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (156)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (170)
<223> n equals a,t,g, or c

<400> 56
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tanggcgcgg tggctcacgc ctgtaatccc cacacnttgg gaaggccgan gcaggcggat 180
cacgaggtca gaagattgag accattctgg ctaacatggt gaacccccat ctctactaaa 240
aatacaaaaa ttagtcaggc gcgatggcgg gcacatgtag taccagctac tcgggaggct 300
gatgcagaag aataacttgg aacctggg 328

<210> 57
<211> 1489
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (710)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1109)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1117)
<223> n equals a,t,g, or c

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<222> (1206)
<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

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<222> (1218)
<223> n equals a,t,g, or c

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<221> misc feature
<222> (1264)
<223> n equals a,t,g, or c

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<221> misc feature
<222> (1311)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1446)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1467)
<223> n equals a,t,g, or c

<400> 57
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ggcatctctt agccgaggcc aacaggaact gcacaagtcc attatagtca aagttagcaa 420
ttttgatacg taaacacaat acttcattct tcctcatctg agctttcctt ccttcttcct 480
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aatgtccatt aatcactcag gcacgagcct ggcactgcca cgtcagcccc cagcatgacc 600
aaacccaggt ttctcttgct tggggctgag aactgtcaga tttttctcat caaaaatgtt 660
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ttaaagctcc agactgttta aaatatacag agggagcagg ggaaagttaa gcatgtgcta 780
gtgtctgaac ccagttcagt ttatctccag ttgaaacgat atacactata ttatgtataa 840
atgtatacac acttcctata tgtatccaca tatatatagt gtatatatta tacatgtata 900
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cagtantcat ntagtcangt gattgattca gttctgctat gaaacattgt aacacgtacc 1260
cacnactgac aactactcgt gagcgttcat taggagtgac ctaactttgc ntgcctgctc 1320
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gctggntgcg ggacacggcc cttctcngtg tcccaggcgc tgcctcatt             1489
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<210> 58
<211> 1283
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (38)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (550)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1242)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1250)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1260)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1263)
<223> n equals a,t,g, or c

<400> 58

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ctgtggagaa aatgcttgta gtaacatatt ttaaatgtac taacaagacc agtcatgggm 180
aaatgtttct gagacaaatc tctagtttat gatttaaaac agtacgtttt cttacgtgac 240
gaaaacaaaa agtgtgttaa tttgttccca gtggttgaag ttatttgcca acaattttac 300
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ctgaggggta agcattttat ttccctttag gaaaaacgtc agctgcttgt aaccactgtg 420
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ttacacaatt gcctctcccc cacaaatcat aattgtttca gtaaaatggt tacttggttt 720
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acaacataat ctagtttaca gaaaaatctt gtgctagaat actttttaaa aggtattttg 1140
aataccatta aaactgcttt ttttttcca gcaagtatcc aaccaacttg gttctgcttc 1200
aataaatctt tggaaaaact maaaaaaaaa aaaaaaaaam mngggggggn gcccggggtn 1260
ccnccggggg gcccaagttt tac 1283

<210> 59
<211> 740
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (696)
<223> n equals a,t,g, or c

<400> 59
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tgctccgctg gacccgagcc tggaggctcc cgcgtgaggg actcggcccc cacggcccta 120
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cccagcagac aggccgtagg tgctgacggt ggatgctcgt aaccacggtg acagcccccca 360
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<210> 60
<211> 1291
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (7)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (147)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1211)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1283)
<223> n equals a,t,g, or c

<400> 60
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cattcggcag ccaatagaat ctaaganatg gcggaaaaat gattccgcct cgggagctaa 180
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<210> 61
<211> 971
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (856)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (886)
<223> n equals a,t,g, or c

<400> 61
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<210> 62
<211> 618
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (563)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (598)
<223> n equals a,t,g, or c

<400> 62
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aattggacat gaataaaact ctagtgggaa aaagttcaaa ggtgattgaa taaataattt 480
aactttgccc tgggtattaa gtccagggct cccagattgt ggagcagagc cttggagagt 540
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ggatggtaaa taattcca 618

<210> 63
<211> 1138
<212> DNA
<213> Homo sapiens

<220>
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<222> (7)
<223> n equals a,t,g, or c

<220>
<221> misc feature
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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (22)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (27)
<223> n equals a,t,g, or c

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<222> (29)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1123)
<223> n equals a,t,g, or c

<400> 63
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atttttataa agtgtttttg agtgtcctat gggccggggc agggtccaag atcttttccc 720
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tctcacacca tgtttttgta cagaactgat ggttgaatct ttgttctctt gaaataaaca 1080
gaagaaaatg aaaccttaaa aaaaaaaaaa aaaaaaaaaa acncgggggg gggcccgg 1138

<210> 64
<211> 418
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (365)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (371)
<223> n equals a,t,g, or c

<220>
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<222> (380)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (391)
<223> n equals a,t,g, or c

<400> 64
tgctcatcca gaggagctca ccacagtcac tgcgacagac tgccacactc accctggcct 60
ggcctcagag aagttgagct actggcctca gttcacacag agcagatgga ggaagagctg 120
gcactaggac ccagggggca ggggggagcc tccctggctg gaagggatgg caggagcgct 180
ggtgcaggta gctatggagc tctggccaac tctgcctggg gaggtcccag gaaggtggcg 240
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actaggacca gggccctggg cctccccaca ctccccatgg agaagctggc ggcctctaac 360
agagncccaa ngggcttggn cggtcctggg ncgtgaaaat gttcaagtgc ccgattga 418

<210> 65
<211> 2836
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2834)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2836)
<223> n equals a,t,g, or c

<400> 65
aagaaaccgc ccattacaca ccccagtaca ccagcagagg aaacttataa cctcgggagg 60
caggtccttc ccctcagtgc ggtcacatac ttccagaaga gcggaccagg gctgctgcca 120
gcacctgcca ctcagagcgc ctctgtcgct gggacccttc agaactctct ttgctcacaa 180
gttaccaaaa aaaaaagagc caacatgttg gtattgctgg ctggtatctt tgtggtccac 240
atcgctactg ttattatgct atttgttagc accattgcca atgtctggtt ggtttccaat 300
acggtagatg catcagtagg tctttggaaa aactgtacca acattagctg cagtgacagc 360
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aaccggttct tcctctcagg ggscaccaca ctggtgtgct gsctgtgcat tcttgtgggg 540
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ccctcattaa agcngn 2836

<210> 66
<211> 2305
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1973)
<223> n equals a,t,g, or c

<400> 66
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cgcgctcatc tgctggagcc cgagcgsgaa cagcttccac gtgttcgacc agggccagtt 120
tgccaaggag gtgctgccca agtacttcaa gcacaacaac atggccagct tcgtgcggca 180
gytcaacatg tatggcttcc ggaaagtggt ccacatcgag cagggcgkcc tggtcaagcc 240
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tgagaacatc aagaggaaag tgaccagtgt gtccaccctg aagagtgaag acataaagat 360
ccgccaggac agcgtcacca agctgctgac ggacgtgcag ctgatgaagg ggaagcagga 420
gtgcatggac tccaagctcc tggccatgaa gcatgagaat gaggctctgt ggcgggaggt 480
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cgggagcctg tcccgtagct ttagg 2305

<210> 67
<211> 1907
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1221)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1655)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1896)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1904)
<223> n equals a,t,g, or c

<400> 67
gacgcccgcc gcctcactgt ttctagcctt cagtggccaa cgttggtagt cattgtgacc 60
tcagcctgaa aatccctgaa attagcatcc aggatatgac agcccaggtg accagcccat 120
cgggcaagac ccatgaggcc gagatcgtgg aaggggagaa ccacacctac tgcatccgct 180
ttgttcccgc tgagatgggc acacacacag tcagcgtgaa gtacaagggc cagcacgtgc 240
ctgggagccc cttccagttc accgtggggc ccctagggga agggggagcc cacaaggtcc 300
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ggacccggga agctggtgct ggaggcctgg ccattgctgt cgagggcccc agcaaggctg 420
agatctcttt tgaggaccgc aaggacggct cctgtggtgt ggcttatgtg gtccaggagc 480
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aaattgacca agataagtat gctgtgcgct tcatccctcg ggagaatggc gtttacctga 780
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tctttggttc tgggaggggt gagggatggg ggtcctgtac acaaccaccc actagttctc 1800
ttctccagcc aagaggaata aagttttgct tccattcwma aaaaaaaaaa aaaaaaaaaa 1860
tygggggggg kccgktaacc caattggcct ttaagngggt ggtntta 1907

<210> 68
<211> 815
<212> DNA
<213> Homo sapiens

<400> 68
gggtcgaccc acgcgtccgt tttttttaag tgtgaatttt ttattgagat aaacaacagc 60
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aaaaatagca gttgtgtttc aatttacctt attctagcaa ttwaagtwgg taacatacaa 180
atagttatwc tgatacaaga tattaaagac atactcagtt ttaatcaact acctctcaag 240
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tatttttaat ttttttcaat aaagatattc ttagatactg aaagaaatag ttaatgagtt 480
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atatcttgta tcagaataac tttgtatgtt accaacttaa attgctagaa taaggtaaat 660
tgatacacaa ctgctatttt taatttagaa ctttgaccta atttgggttt tcaaaaccat 720
tttggctact tgtattcttt atgctgttgt ttatttcaat aaaaaattca cacctaaatg 780
tatacttact aaaaaaaaaa aaaaaaaaaa actcg 815

<210> 69
<211> 1150
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (14)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (20)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (23)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (25)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1150)
<223> n equals a,t,g, or c

<400> 69
ctcgtgcaat tcgngcagan tgntncctgg cctcctttg cttgcccgtg gctgttcctc 60
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tggggtggcc cttggagctg tgccaaagct acacctcggg gtcctagtct caactggcct 180
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gaaaaaaaan 1150

<210> 70
<211> 344
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (287)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (333)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (339)
<223> n equals a,t,g, or c

<400> 70
cgcaggctct gcggccgggt tccttccgcg ggacggggag aaagagagag cgcgaaagag 60
agaggatgtc tctctcagat tggcacctgg cggtgaagct ggctgaccag ccacttgccc 120
caaagtctat tctccagttg ccagagtcag agctgggtga atactctctg gggggctaca 180
gtatttcatt tctgaaacag ctcattgctg gcaaactcca ggagtcggtt ccagaccctg 240
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cggtattcaa cctggctcca catccatgtt ctncggaant cctg 344

<210> 71
<211> 448
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (425)
<223> n equals a,t,g, or c

<400> 71
tcgacccacg catccgaaga tgttcttgct gccccttccg gctgccgggc gagtcgtcct 60
ccgacgtctg ggcgtgaaca gttctgggca cggggtctcg ccgccgcaga catgacgaag 120
ggtcttgttt taggaatcta tagtaaagac aaagaagatg atgtgccaca gtttacgagt 180
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ctggnaatct cttctgtgga aggtggat 448

<210> 72
<211> 2825
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1809)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2093)
<223> n equals a,t,g, or c

<400> 72
gagaaggagg tcgcgcggcc tcatcccggg ccgcgcccca ggccgccgcc ggccccgcgc 60
tcatgaggtt gctcgcgcgc ccccgccgat cgccatggat cggatgaaga agatcaaacg 120
gcagctgtca atgacactcc gaggtggccg aggcatagac aagaccaatg gtgcccctga 180
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aaaaa 2825

<210> 73
<211> 510
<212> DNA
<213> Homo sapiens

<400> 73

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<210> 74
<211> 458
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (382)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (388)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (424)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (448)
<223> n equals a,t,g, or c

<400> 74
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tggncagcca gattcccatc atgggctncc ccataaaa 458

<210> 75
<211> 377
<212> DNA
<213> Homo sapiens

<400> 75

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tagtccacac ctattcatcc atggaccggc acgatggtgt cccgagccac agctcgcggc 180
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gccccagcaa catccct 377

<210> 76
<211> 2070
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (20)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (39)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (88)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2068)
<223> n equals a,t,g, or c

<400> 76
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gctccgctcc cacttcgcca gctctcacgc tctgatatgc atcagccact ggatcctcgg 360
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<210> 77
<211> 997
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (619)
<223> n equals a,t,g, or c

<400> 77
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<210> 78
<211> 1333
<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (1254)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1297)
<223> n equals a,t,g, or c

<400> 78
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<210> 79
<211> 560
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (542)
<223> n equals a,t,g, or c

<400> 79
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gcttttccat acattgtgtg acccttgccc tatgaccctt tggctgacct taccggaagc 120
catgacgaca gcagcctttt gccattagac gcagggtgat ggtgaggatt ccaagggtta 180

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gacaaaactg gttaatctga actaggtgac tgttaccttg cgtgttttgt ggccaaacca 240
ccaccaaaaa cctcacactg tgatgtaagt acttagtgta aaactagtaa acatttttgt 300
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aacttagcga ggtaaatcga ataaaggagc agtcactctc taacagattg taggagaggt 420
ttagttggat ttagtctatt tgacttgccc ttaatttaat tttatggcaa atcacaaatg 480
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<210> 80
<211> 3203
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1116)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1443)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1942)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3188)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3201)
<223> n equals a,t,g, or c

<400> 80

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<210> 81
<211> 1710
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1424)

<223> n equals a,t,g, or c

<400> 81
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<210> 82
<211> 1379
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (280)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1365)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1378)

<223> n equals a,t,g, or c

<400> 82
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<210> 83
<211> 678
<212> DNA
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<222> (648)
<223> n equals a,t,g, or c

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<211> 2803
<212> DNA
<213> Homo sapiens

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<222> (10)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (50)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (517)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (572)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1926)
<223> n equals a,t,g, or c

<400> 84
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tgtcagcaga gtccgtcaga cgtgagaagg gtgggagcgg cggactgtga acgctggtag 360
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<210> 85
<211> 1278
<212> DNA
<213> Homo sapiens

<400> 85
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<210> 86
<211> 2585
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2573)
<223> n equals a,t,g, or c

<400> 86
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<210> 87
<211> 385
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (385)
<223> n equals a,t,g, or c

<400> 87
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actgactaca tcaaagtcta ctacaccttg agaaaacaaa tgaacgaaaa tctattttcc 180
tcattcatta ccccaacaat aataggactc cctatcgtaa ttattatcac tatgtttcca 240
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caaactggag cccggatatt gatan 385

<210> 88
<211> 2500
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (429)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (1088)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2480)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2482)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2491)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2497)
<223> n equals a,t,g, or c

<400> 88
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<210> 89
<211> 1409
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (841)
<223> n equals a,t,g, or c

<400> 89
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<210> 90
<211> 1336
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (49)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1284)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1317)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1333)
<223> n equals a,t,g, or c

<400> 90
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gtcacgtact cttgcaattg cccgcaacct gactcagcag ctccagacca cgtgccacac 420
cctcctgtcc aacatccaag gtgtaccaca gaacatccaa gatcaagcca agcacatggg 480
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<210> 91
<211> 787
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (677)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (725)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (742)
<223> n equals a,t,g, or c

<400> 91
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cgcagatcca gctacctctg ttagccgccc gaagtacaag ttgcagaagc agcttgatag 180
cctcacagcc aggaccccat cagaagggga ggcagggact cagaggcaac aaaagctttc 240
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acaagtg 787

<210> 92
<211> 1657
<212> DNA
<213> Homo sapiens

<400> 92
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ggcgctttgg ttccagagga ggcccaggag gagggttcag gccctttgta ccacatatcc 180
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ggacaatgac tacaggacac aatgtggctg acctggtggt gatactcaag attctgccaa 480

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ggaaaaaaaa aaaaaaaaaa aaacycgggg gttttct 1657

<210> 93
<211> 485
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (478)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (485)
<223> n equals a,t,g, or c

<400> 93
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ctacctrgcc tgacccagtc ggagcctgac atggtggagg gaaagggaga caagtggggc 180
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agattcctga cttaggggtg gcttttgttt acaagatgca agaggggaaa cctgtccccg 300
actcatcgag acaacatgcc cagttatcag ggagtcctgt gtcacaaggt ctgtctctgc 360
cattgtaagc aagtgccttg ggcgagctgg cctctgcccc acagtctcat ctgtacaccg 420
acagggttga tgcctccctc acagggttga gaacaagagc cakttggcca attaaaanaa 480
aaaan 485

<210> 94
<211> 764
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (202)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (565)
<223> n equals a,t,g, or c

<400> 94
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grtggctgga gaaccaggac cccagagagg tggggccact gaggctggtg cagttgcgct 180
cactcatcag catggcccgg angctggggg gcatcgggca taccccagca ggcccctatg 240
acggtgtgtg accaggccas cccagtgacc tttctcctgc tgcacttgga gggaggggac 300
atacacacag tctcccatct ctcctcccct cccccctgggg tggcccaccg catgggtaca 360
gggggttcca ggaatccaaa tccagcatgg cttggaggag ctctgttggt gagaggtcgc 420
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agggcaggca catgtacggg gcatacaagg cacagcgcct gttggaacag gtggctgtgt 540
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agggccgaaa ctcctgtctg ctatcgagcc ctggtgctat gtggccccgg agccacagca 660
caatcatctc agtggcgaag cacaccactt gattctattt ttttttaaca cattaaatct 720
gtttttaaag ataaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 764

<210> 95
<211> 707
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (45)
<223> n equals a,t,g, or c

<400> 95
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ccacgcgtgc catcatggcg caggatcaag gtgaaaagga gaaccccatg cgggaacttc 120
gcatccgcaa actctgtctc aacatctgtg ttggggagag tggagacaga ctgacgcgag 180
cagccaaggt gttggagcag ctcacagggc agacccctgt gttttccaaa gctagataca 240
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ctggcaaata aattcccgtt tctatccaaa agagcaataa aaagttttca gtgaaaaaaa 660
aaaaaaaaaa aaaaaaaggg ggccccccttt tgggggtccc ctggggg 707

<210> 96

<211> 815
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (16)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (45)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (50)
<223> n equals a,t,g, or c

<400> 96
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taaccccccaa agaagaatcc cccccacatt wagccttgtt aagtaaatgc ctcctgaccc 120
caagcccgaa gatgcccccc attctctwag tgatggcggc gttagggttt gagagaaggg 180
aatttggctc aacttcagtt gagagggtgc agtccagaca gcttgactgc ttttaaatga 240
ccaaagatga cctgtggtaa gcaacctggg catcttagga agcagtccct ggagaaggca 300
tgttcccaga aaggtctctg gagggacaaa ctcactcagt aaaacataat gtatcatcat 360
gaagaaaact gattctctat gacatgaaat gaaaatttta atgcattgtt ataattacta 420
atgtacgctg ctgcaggaca ttaataaagt tgctttttta ggctacagtg tctcgatgcc 480
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gattgattga ttactattaa ctacaaggta taatttacta tcaccttatt taaattttat 720
gaattaattt gaatgttttt tacactaact aacttttccc aataaagtcc actatgaaac 780
cacgacaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 815

<210> 97
<211> 658
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (627)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (634)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (635)
<223> n equals a,t,g, or c

<400> 97
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tgcccaagat gctgtacccc gagtaccaca aggtgcacca gatgatgcgg gagcagtcca 180
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ctctgatcga cctcaaatcc ggagttnccc cttnncttgt caaattgacc gcccaata 658

<210> 98
<211> 249
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (248)
<223> n equals a,t,g, or c

<400> 98
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agactscccct tagagataga gaaacagacc caagaaatgt gctcaattgc aatgggccac 120
atacctagat ctccagatgt catttcccct ctcttatttt aagttatgtt aagattacta 180
aaacaataaa agctcctaaa aaatcaaaaa aaaaaaaaaa aaaaaaaaaa aaccccgggg 240
ggggcccng 249

<210> 99
<211> 752
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (612)
<223> n equals a,t,g, or c

<400> 99
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tcgccaggcg cgcctccctg tcggtgcagg accgctactc gccccccaac gccgatggcc 120
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agcccaggag gngacaccgy ccgcccgccg ctcccagacc tcgcccgagt cggctctgtt 660
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 752

<210> 100
<211> 3059
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (14)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (28)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (109)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3019)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3047)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3058)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3059)
<223> n equals a,t,g, or c

<400> 100
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<210> 101

<211> 1682
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (52)
<223> n equals a,t,g, or c

<400> 101
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ctagtgggct cttcccagag tggcagagct gggggagaat ggagaacttg gcctcttatc 180
gatgaattaa gcaacaatgt aactggtctt gacttgtcat attcccccat gcaatcctag 240
gtctgtattg ctcaatttta ggaagccttt gctactccat cagtaggttt agatttgagc 300
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aaggtaatac tttttcagtt cccttcttcc ttccctctca atccactagc tttcatgttg 480
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cccagaatgt tgcttctatt attgtgcaca accattgaga ggtgttacaa gaatgcagtt 1500
aattttaaca tgtgtgatgt gccatggtgg aaaagtacta tcggaataac tctgcagtga 1560
cagaatttga agtttggcta gcatccatac ttttctactg taaatatttc actctcctct 1620
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aa 1682

<210> 102
<211> 938
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (30)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (812)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (913)
<223> n equals a,t,g, or c

<400> 102
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gcttccggct gccgcaggct tcgctggtgc aggtaagctc cgcacactct cggccggtcc 120
cgagtccgac tccctcaagg gtgacgcgag ctctgccctt taaccggaaa cgtctccctg 180
ctcaccccac ccccgcgcag acgcagtgct gagcacacag ctaccggaca aagagtgacg 240
cccggagctg gagttatggc ggctacggag ccgatcttgg cggccactgg gagtcccgcg 300
gcggtgccac cggagaaact ggaaggagcc ggttcgagct cagcccctga gcgtaactgt 360
gtgggctcct cgctgccaga ggcctcaccg cctgcccctg agccttccag tcccaacgcc 420
gcggtccctg aagccatccc tacgccccga gctgcggcct ccgcggccct ggagctgcct 480
ctcgggcccg cacccgtgag cgtagscctc aggccgaagc tgaagcgcgc tccacaccag 540
gccccgccgg ctctagactc ggtcccgaga cgttccgcca gcgtttccgg cagttccgct 600
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ggctgcggcc tgacatccgc accaaggagc agatcgtgga gatgctggtg caagagcagc 720
tgctcgccat cctkcccgag gcggctcggg cccggcggat ccgccgccgc acggatgtgc 780
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<210> 103
<211> 2012
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1993)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2002)
<223> n equals a,t,g, or c

<400> 103
gctggataat tccagcctgt tagctactca caggaacatg cagaattatt ggctccaggg 60
agttttggag aaagaaggtt tacgttttca aacttacaga taacagttga catcaatgct 120
tctctttccc agaacaatct ggagtttgcc agaaaactct gtaaacagga gtcgtgctgt 180
gtgtgaactg taaactcttc tctccaggcg tcgaggggac ctttgcttta ctttgcagct 240
gggctacatc agacgtgtgc attggaaaca taaacttcct taactgggaa aagaatgctt 300
ctctgtcttc maaatarttc tgctatgtga catttttgcc atcatgaatt ttacatcagt 360
gmtagctctt tgttttacgt gtttcattkg gcaggtcaca aaggctcttg gctaccacac 420
atacgtgcat acacacacac acacacacac acacacacac acacactcat aaaggatttt 480

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tttttgaact atatcccaac agaatcgaat ttccattttg ccaagaatta taaaaccctg 600
aggttttaaa attcagtttc ttttctgggg atttaacatg gaaggacttg gagggcaaat 660
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gtgctggagg gaggggattt aattttaatt ttaaaatgtt taggaaattt atacaaagaa 1920
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aaaaaaaaa aanaaaaaaa anaaaaaaaa aa                            2012
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<210> 104
<211> 1094
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (26)
<223> n equals a,t,g, or c

<400> 104
tcctcctggg aagcctggcc tgcctncccc gcaaaaggtg tttttgcgct ggttcaatga 60
atagatgatg cagaggcccc attggagaca cgtgaatggc gtgtgcggcc atcagttccc 120
ggctgggggg caggtgttgc ttcggccccc gccctccggc cggcgtgtgc gagtgcgccc 180
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gtgactcctg agtgggtgac gcgcagacgg gatttctcag gtcatttgta tggtcgacat 300
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ctggggtgca ctttagtttg gggcgggacg ggagccgccg ttgtgactgg cgtggtctgg 480
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ggctctgact cggctcccta ctccctgcac ccagctgggc gcacttgggg cctgcggtct 600
gaatgtatcc ctcccctcag ttttaacctg agctgccgaa cgcacagtgg gccgggggcg 660
aggctggggg aagcggggcc caattacgga tcccgggagt tacaggtgcc gacgtgatgt 720
cgcttctctg gtgcccagct cccttcctgg tctgagacta gctctggggg tggcgggggc 780
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ttgcggagag ccgcttatgg gtgtggtccg tccagacacc ttgtttcaag ggggatgggc 960
gtgagcgggc aagcagagca tccccaccgc tgagcaagaa ctttttcttg tttttaaacc 1020
atcacgtcct catttcacat tggaataaag tgagtttttg aaacctgcga aaaaaaaaaa 1080
aaaaaaaaaa attc 1094

<210> 105
<211> 2297
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (30)
<223> n equals a,t,g, or c

<400> 105
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tcctgcacca tctgcctaat tccttcctca cagtctgtag ccatctgata tcctagggga 120
aaaggaaggc caggggttca catagggccc cagcgagttt cccaggagtt agagggatgc 180
gaggctaaca agttccaaaa acatctgccc cgatgctcta gtgtttggar gtgggcagga 240
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tgcttccttc ttgcccagcg ctgggttctc tccacccagt aggttttctg ttgtggtccc 360
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cagggctttt gacggagaca gcaaataggc ctctgcaaat caatcaaagg ctgcaaccct 480
atggcctctt ggagacagat gatgactggc aaggactaga gagcaggagt gcctggccag 540
gtcggtcctg actctcctga ctctccatcg ctctgtccaa ggagaacccg gagaggctct 600
gggctgattc agaggttact gctttatatt cgtccaaact gtgttagtct aggcttagga 660
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caaacagcca tgcatctata aaggtcatca tcttctgcca cctttactgg gttctaaatg 780
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tgcgttgtaa gacagaatac gggtttaatc tagtctaggc accagatttt tttcccgctt 1080
gataaggaaa gctagcagaa agtttattta aaccacttct tgagctttat ctttttttgac 1140
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aagatctagt ccaatctttt tctagagaaa aagataatct gaagctcaca aagatgaagt 1620
gacttcctca aaatcacatg gttcaggaca gaaacaagat taaaacctgg atccacagac 1680
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actggaattt actgagaaac ttgtttgtaa aaactatagt taataattat tgcattttct 2220
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aaaaaaaaaa actcgta 2297

<210> 106
<211> 442
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (419)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (423)
<223> n equals a,t,g, or c

<400> 106
tcgacccacg cgtccgcctg tgggacgcgg tggtggccgt tgggtcggga gagtgagcgg 60
tatttgcmtc gtttttcttg cttgttttcc ccccgttaga ctttgtcggt agagcgcggt 120
tatgggccgc aagaagaaga agcagctgaa gccgtggtgc tggtattgta atagagattt 180
tgatgatgag aagattctta tacaacacca aaaagcaaaa cattttaaat gtcatatatg 240
tcataagaag ttgtacacag gacctggctt agctattcat tgcatgcagg tgcataaaga 300
gacaatagat gctgtaccaa atgcatacct gggagaacag acatkgattg gaaatatatg 360
gtatggaarg tattccagaa aaagatatkg atgaaagaag acgacttctt ggaacagana 420
acnccagaga gtccaaaaaa ag 442

<210> 107
<211> 1019
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (995)
<223> n equals a,t,g, or c

<400> 107
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cgacggctcg agtgcggatg gggccgcggt gcgcccaggc gctctggcgc atgccgtggc 120
tgccggtgtt tttgtcgttg gcggcggcgg cggcggcggc agcggcggag cagcaggtcc 180
cgctggtgct gtggtcgagt gaccgggact tgtgggctcc tgcggccgac actcatgaag 240
gccacatcac cagcgacttg cagctctcta cctacttaga tcccgccctg gagctgggtc 300
ccaggaatgt gctgctgttc ctgcaggaca agctgagcat tgaggatttc acagcatatg 360
gcggtgtgtt tggaaacaag caggacagcg ccttttctaa cctagagaat gccctggacc 420
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cttacctgca ggagaagctc ggggccagcc ccttgcatgt ggacctggcc accctgcggg 540
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gctctggtct gatggcaccc agggaagtcc tcacaggcaa cgatgaggtc atcgggcagg 660
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aaaaacagcc agtatcacct gtgatccatc ctcctgtgag ttacaatgac accgctcccc 840
ggatcctgtt ctgggcccaa aacttctctg tggcgtacaa ggaccagtgg gaggacctga 900
ctcccctcac ctttggggtg caggaactca acctgactgg ctccttctgg aatgactcct 960
ttgccagcty tcactgacct atgaacgact ctttngtacc acagtgacat taaagttat 1019

<210> 108
<211> 711
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (642)
<223> n equals a,t,g, or c

<400> 108
cttgaaaact tagtttacta tacatcttgc cctattaata tgttctctta acgtgtgcca 60
ttgttctctt tgaccatttt cctataatga tgttgatgtt caacacctgg actgaatgtc 120
tgttctcaga tcccttggat gttacagatg aggcagtctg actgtccttt ctacttgaaa 180
gattagaata tgtatccaaa tggcattcac gtgtcactta gcaaggtttg ctgatgcttc 240
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aacgggatga ggtgttacag ctgcctccct cttcatgcaa tctggtgagc agtggtgcag 360
gcggggagcc agagaaactt gccagttata taacttctct ttggcttttc ttcatctgta 420
aaacaaggat aatactgaac tgtaagggtt agtggagagt ttttaattaa aagaatgtgt 480
gaaaagtaca tgacacagta gttgcttgat aatagttact agtagtagta ttcttactaa 540
gacccaatac aaatggatta tttaaaccaa gtttatgagt tggttttttt cattttcyat 600
ttgtatttta ttaagagtgc ttttcttatg gtgatttttt tnaattgcga tttgatatgg 660
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<210> 109
<211> 743
<212> DNA
<213> Homo sapiens

<400> 109
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agcatgggat attttaatag tattatacat aatattttta catagaaaac tttacatagc 120
atttcatatt atataattct gcttattctt tcaaaaattt atacatccat tgggcaagga 180
atggttttca ttaaattacc aatattaaat gcacttaatc attgtgtata ggttaaacca 240
aagtaactat taactaactt ttaggcattt taaggaggta aaacatacat tttacacata 300
aatatttgat gcaaatatgc agataaaatt ttttaaaaat tagaacactg agtaaaacac 360
ctttgataga ttatattgtt ttgttttgag agcaaggatt tccagatatg ttcattcttt 420
aaaacactca gctttggttt ctttgtttcc caaactgcaa agctgctgat aacaaaactc 480
caggattcca tgtgagttca gctatgtcta ctttaacaca aatattaaaa cagaattcag 540
raaatgcagt attaaggatc cagcttctat tgaaaccaat atccatttgc atcataacaa 600
caaacatttg aatgagatgg tcacacttgt acttatcagc aggttccttt aataacaaag 660

actactaaat gtatatcctt aatcacaaaa gaacaacaaa aaaaatacag gttttttttt 720
tttcatttcg tacaaaagtc acc 743

<210> 110
<211> 795
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (645)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (737)
<223> n equals a,t,g, or c

<400> 110
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tatttgtatt acaaagaact tgaaatttac tttcttagtt gattatatta aatgatgtat 120
atattatatg tggtttataa gctcaacact ggccattttt ttagttttat tgttaaatgg 180
tatttttcta tgtttaatta taatagatct ggctttttct ggatagcata aagatcactg 240
aactatatat atataagara caagagttct attttagcac aaaggcattt tatattattt 300
attgaatcca taagtttgtt ttcgtcaaaa acattccata ttatttctgc tcctttttat 360
ttgtatagtt tgttatttaa agaaatggca gtccttcctg ttcttaatac aataaaattg 420
aaataatgca cctagtaatg tggccgacat ctcttctcac caccatggac tgttttcaac 480
aacagttgat cttctggtct gtgctgagag gcgcatgcat gtctttcgtc acgtcgggca 540
gcacacctgc tgtgaaatac tgctttcatc tacctcttca gaaggcttct tgcttgttga 600
caagtaccgc aaaggcttta ttctggactg gctatctcat aaaanggatt tctgtaagac 660
tttgcagtgt cattccctca gaaccyaggt ttgtttctaa agccacggta ttgtccrrgr 720
rcccctgtgt ktggggncag gtagctatcc ctcccatgtc attagtaatc ctttaggatt 780
ttaaggtaca atggg 795

<210> 111
<211> 1332
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1194)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1237)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1241)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1300)
<223> n equals a,t,g, or c

<400> 111
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cccccaggga cacaacccct ggtcttggac cagtagagga cacggagggt tcagacccct 120
cctcagaccc tccccacatc tgaaactgcc tccccccaac caccagcagc agcagggccc 180
tcctccccca ccagctctcc ccacagggcc cctcagcatc atggagaccc gcagcggggc 240
ttagccaccc ctcaaaccca gggccccctg gcacctgggc tctggccgtg ttttctggcc 300
agagccccac tttcctaact cgtgctccct tccgccttct tttccgtact gtgaagaaag 360
aactctccac cccagctccc accctgccct ggcctgggtg gaggaactgt gcctccatcc 420
ccagaagaaa cagcccctc tgctgctggg gtgggactgt ctgtgtgccc tgtgggggtc 480
cgtgtgagca ggcccacctg gctccagacc cgcccccaac ctgagacaga accaggctga 540
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aggcctggta ccgsctcacc cacagaggtc tgtgccaggt gcgcttctgc aggtggagcc 660
aagctctccc tgaggccaga ggcggggcct gggccgggag cccaggggaa ggccaggctg 720
gaccccggct ycacacccac atccagcctg caggcctctc tgcagtcctc tcaccctccc 780
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acggggagcc ctttcttccc tggaccctgg ggcttgnttc ntgggggggc tcttccaaga 1260
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aaggcaaaag ag 1332

<210> 112
<211> 743
<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (53)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (272)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (275)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (278)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (590)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (618)
<223> n equals a,t,g, or c

<400> 112
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ggtaacggcc tccaccgacg ggatcggctt cgcatcgccc ggcgtttggc ccaggacagg 180
gccacgtggt cgtcagcagc cggaagcagc agaatgtgga ccaggcggtg gcacgctgca 240
rggggagggg ctgagcgtga cgggcacctg tncantgntg gggaaggcgg aggaccggga 300
gcggctggtg gccacggctg tgaagcttca tggaggtatc gatatcctag tctccaatgc 360
tgctgtcaac cctttctttg gaagcataat ggatgtcact gaggaggtgt gggacaagct 420
ctggatggac aaggaaaaag aggaaagcat gaaagaaacc ctgcggataa gaaggttagg 480
cgagccagag gattgtgctg gcatcgtgtc tttcctgtgc tctgaagatg ccagctacat 540
cactggggaa acagtggtgg tgggtggagg aaccccgtcc cgcctctgan ggaccgggag 600
acagcccaca ggccagantt gggctctagc tcctggtgst gttcctgcat tcamccaytg 660
gsctttccc acctytgytc amcttactgt tcacctcatc aaatcagttc tgccctgtga 720
aaagatccag ccttccctgc cgt 743

<210> 113
<211> 1690
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1659)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1664)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1676)
<223> n equals a,t,g, or c

<400> 113
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ttggctgcag tccagctgcc agatggcttc aacctgctct gcccaacccc accacctccc 120
ccagacacag gccccgagaa gctgccatca ctggagcacc gggactcccc ttggcaccga 180
ggccccgccc ctgccaggcc taaaatgctg gttatcagtg gaggtgatgg ctatgaggac 240
ttccgactca gcagtggggg cggcasagca gtgagactgt gggtcgagac gacagcacaa 300
accacctyct cctgtggagg gtgtgaccct gtctgccgtg gcccaggact sgcccgccca 360
cctgccttca gcctgcttgc ctctccctag cccacacgca gactttgacc aggagtatcc 420
agccagggga cacatgtgcy kgcrtgggct ctgcttgtct tcgcggaaga ttcctgatgg 480
aacacccact ggccagccag gccatggctt ctcccgaccc tctggctgcc ccggtgcttc 540
cagtcatgat cgggtggggg acatgtgggc tgaccaggac ctctgaccct ggagcttcta 600
ccaaagacac agctgggtct ggaccccacg ggsstgggga gggccatgtg caatatttgg 660
agggtttctt ggagggcagc aggaaggctg gggaattccc catgtacagt atttatgttt 720
ctttttagat gtgtaccttc ccaagcactt atttatgcag tgacctggtc acctggggtg 780
ggggtgattt gaggaaatga catgaggaaa agaaacctat tcctgccctg gggaccaccc 840
tgggactcta accaagcctt cctggaggga cccatgcgcc cctgagcccc attccattca 900
tacagacaca cacgtacgca cactgcatgt ccaaggccct aaacattgcc cgttgacata 960
aactttccag ggccccagcc tgatggggct gccctcagtc ctctagatca agatgctgac 1020
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tggtggtgcc tttagtggtt ccctaatttg ggaacactga tggggccttg gacagggctt 1140
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tgcttccctg tgtctcatgc actggcacat atggtcacct tggagggcag acctaggagc 1260
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tttggttttg tttggggtgg gtgggtcatt gcggtcttag attatgtttc tcttgctacc 1560
aaacagtcat gtattaactc tctttggatg atgaagttta aagagtcaat aaatagaaac 1620
accagatgac tgcaaaaaaa aaaaaaaaaa aaaaaaaana aaanaaaaaa aaaaanaaaa 1680
aaaaaaaaaa 1690

<210> 114
<211> 620
<212> DNA
<213> Homo sapiens

<400> 114
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gccagctgac tgagggtaca caggattggg tctagacctt gatgcctggg tggagggccc 120
ttgtaagggg ccatagcctc ttcaggacca actggaggga gagttaggaa acaccagctc 180
ctgcctgggg cagtgaggga atgggagcag ctgtgggcgc ctcatttcag gcaagtcctc 240
cccaaacctt cagatgcagt gagacctggc cttcctgttg tgcttttcag actttgtttt 300
cagaatgctt ttatctcgag tgtgcccttc ggccctcaca agagcccctg ggagtaggt 360
ggtggcctgt gccgtcatcc ccatttcaaa gcagggagct gaggtcctgg gaggggaaag 420
tgcttgcctg aggtcccact gtgttagtgg gtgggcagga ctggaactcg gttctccaac 480
agcccagagc tcactctttt acacccagag gtggagcagg tggcttaggg ggtggttatg 540
tacttcacaa gccaattccc ttcagccagg agctcctggg tgcatttccg tgtcagaaac 600
agtaccgagt cccacccct 620

<210> 115
<211> 542
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (392)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (412)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (511)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (521)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (535)
<223> n equals a,t,g, or c

<400> 115
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cctctactcc agcctccact ccggcctcca ccatgtccgt caggtgaccc agaagtccta 120
caaggtgtcc acctccggcc cccgggcctt cagcagccgc tcctacacca gcgggcctgg 180
ctcccgcatc agctcgtccg ccttctcccg ggtgggcggc asttccgggg gggcctgaac 240
agcagcatga gtgtggtcgg gggctacggc ggcggggccg gggtatgggg ggcatcacgg 300
ccgtctcagt gaaccagagc ctgctgagcc cccttwaagc tggaatkgga tcccaacatc 360

caagctgtgc gcaacccagg agaaggagca gntcaagacc ttcaacaaca anttggcttc 420
gttcatcgac aagtgaagca ctggagcagc agaacaaatt tttggagacc aattggagct 480
tcttaaagca gcagaagacg cgcggagaac ntagacaaat nttcgagagt aaatnagaac 540
tt 542

<210> 116
<211> 525
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (420)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (424)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (517)
<223> n equals a,t,g, or c

<400> 116
aattcaaccg tcgttatccc aaaattcagt tttcactttc caccggccct tccggcacta 60
tgctggatgg tgtactggag ggaaaactga atgcggcgtt tattgatgga cccattaacc 120
atactgccat cgacgggata ccggtatacc gcgaggaact gatgatcgtc acgccacaag 180
gatatgcgcc agtaacccgt gccagtcagg ttaatggcag taacatttat gccttccgcg 240
ccaattgttc gtatcgtcgc cacttcgaga gctggtttca tgctgacggt gccgctccgg 300
gaactatcca tgagatggag tcttatcacg gaatgttggc ctgtgtgatc gcaggagcag 360
gcattgcgct tattccgcgc tctatgctgg aaagtatgcc ggggcatcac cargttgaan 420
cgknggccgt tagctgagca atggcgttgg ttaacaacct ggctggtctg gccgtcgtgg 480
tgcgaaaaaa cgttccgctc gaagggggc ccggtancca attcg 525

<210> 117
<211> 728
<212> DNA
<213> Homo sapiens

<400> 117
aacgagcgcc tgctaggatc agcggtggtg gttccgcgat ggtaggcggc ggcggggtcg 60
gcggcggcct cctggagaat gccaaccccc tcatctacca gcgctctggg gagcggcctg 120
tgacggcagg cgaggaggac gagcaggttc ccgacagcat cgacgcacgc gagatcttcg 180
atctgattcg ctccatcaat gacccggagc atccactgac gctagaggag ttgaacgtag 240
tagagcaggt gcgggttcag gttagcgacc ccgagagtac agtggctgtg gctttcacac 300
caaccattcc gcactgcagc atggccaccc ttattggtct gtccatcaag gtcaagcttc 360
tgcgctccct tcctcagcgt ttcaagatgg acgtgcacat tactccgggg acccatgcct 420
cagagcatgc agtgaacaag caacttgcag ataaggagcg ggtggcagct gccctggaga 480
acacccacct cttggaggtt gtgaatcagt gcctgtcagc ccgctcctga gcctggcctt 540

tgacccctca gcctgcatac tggtatcctg gtcccagctc ctgccagggc tgttaccgtt 600
gttttcttga atcactcaca atgagaaact aacattttgc tttttgtaat aaagttaatt 660
tatattcarw tcaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa acccgggggg 720
gggccccc 728

<210> 118
<211> 948
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (920)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (944)
<223> n equals a,t,g, or c

<400> 118
agaagtacgg accccctgaag cccctgccac agaccccgca cctggaggas gacttgaagg 60
aggtgctgcg ttctgaggct ggcatcgaac tcatcatcga ggacgacatc aggcccgaga 120
agcagaagag gaagcctggg ctgcggcgga gcccatcaag aaagtccgga agtctctggc 180
tcttgacatt gtggatgagg atgtgaagct gatgatgtcc acactgccca agtctctatc 240
cttgccgaca actgcccctt caaactcttc cagcctcacc ctgtcaggta tcaaagaaga 300
caacagcttg ctcaaccagg gcttcttgca ggccaagccc gagaaggcag cagtggccca 360
gaagccccga agccacttca cgacacctgc ccctatgtcc agtgcctgga agacggtggc 420
ctgcgggggg accagggacc agcttttcat gcaggagaaa gcccggcagc tcctgggccg 480
cctgaagccc agccacacat ctcggaccct catcttgtcc tgaggtgttg agggtgtcac 540
gagcccattc tcatgtttac aggggttgtg ggggcagagg gggtctgtga atctgagagt 600
cattcaggtg acctcctgca gggagccttc tgccaccagc ccctccccag actctcaggt 660
ggagcaacag ggccatgtgc tgccctgttg ccgagcccag ctgtgggcgg ctcctggtgc 720
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cgtcagcttc tcccaagccc acgtcaggcc tggcctcatc tcagaccctg cttaggatgg 840
gggatgtggc caggggtgct cctgtgctca ccctctcttg gtgcattttt ttggaagaat 900
aaaattgcct ctctctttgn aaaaaaaaaa aaaaaaaaaa gggnggcc 948

<210> 119
<211> 211
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (123)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (125)

<223> n equals a,t,g, or c

<400> 119
tcgacccacg cggtccgctt ggtggggtcg gctgctttct cgcgtttccc cccaaccccg 60
tccggcctcg cccagcgttt ccacgcggaa ccaactgcca gaggcgcggc gcggcgtcga 120
gcngngcgag tgtgaggaaa ccgccgcctc agccgagcgc gcgggcccgc ccagggcgtt 180
agttttcggc gcgcagtcgc ggtcccccgg c 211

<210> 120
<211> 1308
<212> DNA
<213> Homo sapiens

<400> 120
tcgacccacg cgtccggact gttctaagtg agttcgggtg ggggagcttc acgaggggag 60
gctgctctgt gaaggaaccg cctttctctc cgcgtgtctc accctttttct ccccatatct 120
gtttggacat gagctgaggg cacggtcgcg ggcggtcagc ctgttcgcag ctacggcgag 180
gaggggcgcg attgytcctt gttgccgctc cgcttagtgg ccgcgtccat tccgcgcggt 240
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catggccccg ctgggaggcg ccccgcggct ggtactgctg ttcagcggca agaggaaatc 360
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ccagcccatc tggctggtga gtgacacacg gagagtgtct gacatccagt ggtttcggga 660
ggcctatggg gccgtgacgc agacggtccg cgttgtagcg ttggagcaga gccgacagca 720
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ctggccgagg tgaggaacag acaggggggg tctagattct gaggggggttg gtggatattg 1020
ggcaaggcag gaaacctctg gagacctcat ttctccatgg gggaagacag ccatgctctt 1080
caggaggaga ctccaagggc aaaggagggt gtcttggctg tgcttgaagg cgaaaccctg 1140
ccatatcccc agtgccagtc ccctcagcct gtggtggcct tgcatcctga ctggatgttc 1200
tcagcccctt gttctgggca agaacccaga gctccccagt gtggatacta ataaacctct 1260
tggagcacaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaagg 1308

<210> 121
<211> 2516
<212> DNA
<213> Homo sapiens

<400> 121
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attacaaaat attctaaaag ggtttttttgt ggtacttcaa gaaacctgat tagttttgat 120
ctattgaaat cacaaaagta gaacagggcw ytttattttt gtataattta ggattaggta 180
tgcttctttg ttctaacaag tcatgttttc taacccttct ttcactaagc aaaccagaac 240
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tgccgtagtg ttattcttgt atgccaaatc tttttttccc caaaattagc actttaattt 360
tatttactgt tataatattt gttttcttag attaggtagg aaatcttaat ttggccaccg 420
cctactttga caagtaaata ttacatcata cgattttgca acattaaatt agaacactag 480

aaactaaaaa attatgtttc agtgaatgct acaactaagc attttttttt tttaagaaaa 540
acaattgtat tatgttttgt tgccttgcca ctttgagtat cttatctgaa aatctgttcc 600
ttgccatgtt tttctcctgt taacataaac tatgtgccct gtgaatttct ggggactgaa 660
tttgaaattg ctcctgccaa ccgtttgtgg cctggcgtgt atctgaatgc ctgaatatct 720
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atgtatagaa tatttttcaa cacttattaa cttttcagat aacataatct atatatagat 960
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tccatttctt ttggtggggg ggattgtatt tttgctttct ttagaaatgt aatgtttgtt 1080
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tgatggtgtt gaccaataaa atatctagtg ataaggaaat ttgtagcatc aactagaata 1200
atctacattg atagcattta ttgtgataag tacattgttt ccacttcttg atatgactga 1260
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cttatttgtg cagtctgact acacagaggc gtataatccc aaaataaaac gtgatgaacg 1740
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acatcacagt acattggtat ctacaagaca ttatagagca cctgaagtta ttttagccct 1860
agggtggtcc caaccatgtg atgtctggag cataggatgc attcttattg aatactatct 1920
tgggtttacc gtatttccaa cacacgatag taaggagcat ttagcaatga tggaaaggat 1980
tcttggacct ctaccaaaac atatgataca gaaaaccagg aaacgtaaat attttcacca 2040
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acctctgaag gaatttatgc tttctcaaga tgttgaacat gagcgtctct ttgacctcat 2160
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gagatcttac agactgtatc agtctaattt ttaaatttta agttattttg tacagctttg 2340
taaattctta acatttttat attgccatgt ttattttgtt tgggtaattt ggttcattaa 2400
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<210> 122
<211> 1139
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1053)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1124)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (1125)
<223> n equals a,t,g, or c

<400> 122
gtggcgcacg gggtgggagc ggacccaggc cgggagcagg cgccgccgcc agtgagaacc 60
ggggccggag ccgggtgcgg atttgctggg gctgagtcgg gggcgcgcgg gccctgacct 120
ctgccctctg acctctcccc tagcaggcga ccatggggaa cgtgttggct gccagctcgc 180
cgcccgcagg gccgccaccg ccgcctgcgc cggccctcgt ggggctgccg ccacctccgc 240
cctcgccgcc gggcttcacg ctgccgccgc tgggaggcag cctgggcgcc ggcaccagta 300
cgaktcgarg ttcggaacgg acccccgggg ctgcaaccgc cagcgcctca ggggccgccg 360
aggatggggc ctgcggctgc ctgcccaacc cgggcacatt cgaggagtgc caccggaagt 420
gcaaggagct gtttcccatt cagatggagg gtgtcaagct cacagtcaac aaagggttga 480
gtaaccattt tcaggtcaac cacacagtag ccctcagcac aatcggggag tccaactacc 540
acttcggggt cacatatgtg gggacaaagc agctgagtcc cacagaggcg ttccctgtac 600
tggtgggtga catggacaac agtggcagtc tcaacgctca ggtcattcac cagctgggcc 660
ccggtctcag gtccaagatg gccatccaga cccagcagtc gaagtttgtg aactggcagg 720
tggacgggga gtatcggggc tctgacttca cagcagccgt caccctgggg aacccagacg 780
tcctcgtggg ttcaggaatc ctcgtagccc actacctcca gagcatcacg ccttgcctgg 840
ccctgggtgg agagctggtc taccaccggc ggcctggaga ggagggcact gtcatgtctc 900
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tgcacgcaac atactaccac aaagccagtg accagctgca ggtgggtgtg gagtttgagg 1020
ccagcacaag gwtgcaggac accagcgtct ccnttsgggt accagcttgg aacttgccca 1080
agggccaacc tcytctttca aaggstctgt tgggataagc aaanngggat tcgtggggt 1139

<210> 123
<211> 2114
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1966)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2039)
<223> n equals a,t,g, or c

<400> 123
accccgcgcg ccactcgctc gcgtcmgagg gaggagaaag tggcgagttc cggatccctg 60
cctagcgcgg cccaaccttt actccagaga tcatggctgc cgaggatgtg gtggcgactg 120
gcgccgaccc aagcgatctg gagagcggcg ggctgctgca tgagattttc acgtcgccgc 180
tcaacctgct gctgcttggc ctctgcatct tcctgctcta caagatcgtg cgcggggacc 240
agccggcggc cagcggcgac agcgacgacg acgagccgcc ccctctgccc cgcctcaagc 300
ggcgcgactt cacccccgcc gagctgcggc gcttcgacgg cgtccaggac ccgcgcatac 360
tcatggccat caacggcaag gtgttcgatg tgaccaaagg ccgcaaattc tacgggcccg 420
aggggccgta tggggtcttt gctggaagag atgcatccag gggccttgcc acatttgcc 480
tggataagga agcactgaag gatgagtacg atgacctttc tgacctcact gctgcccagc 540
aggagactct gagtgactgg gagtctcagt tcactttcaa gtatcatcac gtgggcaaac 600

tgctgaagga gggggaggag cccactgtgt actcagatga ggaagaacca aaagatgaga 660
gtgcccggaa aaatgattaa agcattcagt ggaagtatat ctatttttgt attttgcaaa 720
atcatttgta acagtccact ctgtctttaa aacatagtga ttacaatatt tagaaagttt 780
tgagcacttg ctataagttt tttaattaac atcactagtg acactaataa aattaacttc 840
ttagaatgca tgatgtgttt gtgtgtcaca aatccagaaa gtgaactgca gtgctgtaat 900
acacatgtta atactgtttt tcttctatct gtagttagta caggatgaat ttaaatgtgt 960
ttttcctgag agacaaggaa gacttgggta tttcccaaaa caggtaaaaa tcttaaatgt 1020
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aaacagagct cagctgcaaa aaagcatatt ttctgtgttt ctggactgca ctgttgtcct 1260
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tggttatttg gttattttac tcaattggtt actctcattt gaaatgaggg agggacatac 1500
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tattctgttg ttataaaact atacccactg caaaagtagt agtcaagtgt ctaggtcttt 1680
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tggtcagtta ataaaaatgg ttttacccac taaaaaaaaa aaaaaaaggg cggccgctct 1920
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tagtgagtcg tattataagc taggcactgg ccgtcgtttt acaacgtcgt gactgggana 2040
tctgctagct tgggatcttt gtgaaggaac cttacttctg tggtgtgaca taattggaca 2100
aactacctac agag 2114

<210> 124
<211> 583
<212> DNA
<213> Homo sapiens

<400> 124
gcccggccta ttcccttggg cttttaaaaa gcgtcttgga tggaggtggt gcaggtgctc 60
accaagcccg cagtaaccca agttgcatgt atccccaggg cacttttgtg attcccctgc 120
ttgtgactgc acaccgggac cccactcaat tcaaagaccc agactgcttc aaccctacca 180
acttcctgga caagggcaag ttccagggca atgatgcttt catgcccttt gcctcaggtg 240
caggcagagg aggaaggggga ccagcctgga ctggctctgg ggtacctggt gctcactgtg 300
cacctgtgta cccggcaaag cagatgtgcc tgggcacagg cctggcccac tcgggtatct 360
tcctattcct tacggccacc ttacagaggt tctgcctgct ccctgtggta cgccctggca 420
ccatcaacct cacctgcagt gcactggcct gggcagtgtc cccccagact tccagctcca 480
gccagtggcc tgctgaggtc aggctccact atggtgggct cactggccct caaacctcca 540
taccctccts ggtcaataaa ggccctaaat tgcaaaaaaa aaa 583

<210> 125
<211> 1987
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature

<222> (7)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (14)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (517)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1960)
<223> n equals a,t,g, or c

<400> 125
cagtacngtc cgantcccgg gtcgacccac gcgtccgatg gcggcggagg aacctcagca 60
gcagaagcag gagccgctgg gcagcgactc cgaagtgtta actgtctggc ctatgatgaa 120
gccatcatgg ctcagcagga ccgaattcag caagagattg ctgtgcagaa ccctctggtg 180
tcagagcggc tggagctctc ggtcctatac aaggagtatg ctgaagatga caacatctat 240
caacagaaga tcaaggacct ccacaaaaag tactcgtaca tccgcaagac caggcctgac 300
ggcaactgtt tctatcgggc tttcggattc tcccacttgg aggcactgct ggatgacagc 360
aaggagttgc agcggtgaga agggtgggca ctgggcaccg aggcaggtgg gtgtytacct 420
cctccccggg cgagtaggat gtgtctcgag tagggtgtct ycctccttcc cgggcgatgg 480
gctggactct ggccttgcca rgcggggcag tgctgtntcg gccctggcgt ctgggctggt 540
cgaggagccc atgctgggcc cgcctttcca tcccaccccc aggttcaagg ctgtgtctgc 600
caagagcaag gaagacctgg tgtcccaggg cttcactgaa ttcacaattg aggatttcca 660
caacacgttc atggacctga ttgagcaggt ggagaagcag acctctgtcg ccgacctgct 720
ggcctccttc aatgaccaga gcacctccga ctaccttgtg gtctacctgc ggctgctcac 780
ctcgggctac ctgcagcgcg agagcaagtt cttcgagcac ttcatcgagg gtggacggac 840
tgtcaaggag ttctgccagc aggaggtgga gcccatgtgc aaggagagcg accacatcca 900
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ctctgcattg cctgcctttt tgccttcacc tcttttcttc cccgccccct gcacattcgg 1860
gktctcagcc cccaggctgt gagctccttg ggcaggcccc tcaataaatg tgaaactgct 1920

gctgcaaaaa aaaaaaaaaa aaaaaaaggg ggccgcttan agatcctcaa gggccaagta 1980
cggtgat 1987

<210> 126
<211> 1451
<212> DNA
<213> Homo sapiens

<400> 126
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gcccgtctgg taaacttgtc cagattgaat atgctttggc tgctgtagct ggaggagccc 120
cgtccgtggg aattaaagct gcaaatggtg tggtattagc aactgagaaa aaacagaaat 180
ccattctgta tgatgagcga agtgtacaca aagtagaacc aattaccaag catataggtt 240
tggtgtacag tggcatgggc cccgattaca gagtgcttgt gcacagagct cgaaaactag 300
ctcaacaata ctatcttgtg taccaagaac ccattcctac agctcagctg gtacagagag 360
tagcttctgt gatgcaagaa tatactcagt caggtggtgt tcgtccattt ggagtttctt 420
tacttatttg tggttggaat gagggacgac catatttatt tcagtcagat ccatctggag 480
cttactttgc ctggaaagct acagcaatgg gaaagaacta tgtgaatggg aagactttcc 540
ttgagaaaag atataatgaa gatctggaac ttgaagatgc cattcataca gccatcttaa 600
ccctaaagga aagctttgaa gggcaaatga cagaggataa catagaagtt ggaatctgca 660
atgaagctgg atttaggagg cttactccaa ctgaagttaa ggattacttg gctgccatag 720
cataacaatg aagtgactga aaaatccaga atttcagata atctatctac ttaaacatgt 780
ttaaagtatg ttttgttttg cagacttttt gcatacttat ttctacatgg tttaaatcga 840
ctgtttttaa aatgacactt ataaatccta ataaactgtt aaacccacct tccagccttt 900
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actayattgc caagcagaat gatgaaatga ctttttcgtt gtcaggcaat tttggttaag 1020
tcaaatctta atgccctctt cgctatcaga tgttgcctgt gtttccataa agcaaaatgc 1080
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ttcatggaac aagaaaagaa gcataggtac ttttaggtgc cattaggtat tgatcagtga 1200
aatcctaggg tgctctatga gattgtacta ggcctatgaa gagtggtaag ccaaataggt 1260
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ctccacaagt aggtaaacat gtttaaagga acccgggttc ttagattttg ttagactttt 1380
taaactcaag gatgagcata agtgcttgaa ataaaatgct aatacttaag tgtcaaaaaa 1440
aaaaaaaaaa a 1451

<210> 127
<211> 1234
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (857)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1204)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (1226)
<223> n equals a,t,g, or c

<400> 127
aggttcccag ctagccagta aattctttaa agacaagcat tgtacccttt gcctcagtgt 60
gcccagcacc aacctggcac atgctctatt catgttttcc atgagtgttt catgttagag 120
gtgtattttg tacacaggtt ttatgctggg ggctcagaga gaagtggaca gcagattgtt 180
ggccctccca ggaagaaaag tcccaacgag ctggtgggat gatctcttta aaggtgccaa 240
agagcatgga gctgtagctg tggagcgagt gaccaagagc cctggagaga ccagtaaacc 300
gagaccattt gcaggaggtg gctaccgcct tggggcagca ccagaggaag agtctgccta 360
tgtggcagga gaaaagaggc agcattccag ccaagatgtt catgtagtat tgaaactctg 420
gaagagtgga ttcagcctgg ataatggaga actcagaagc taccaagacc catccaatgc 480
ccagtttctg gagtctatcc gcagagggga ggtgccagca gagcttcgga ggctagctca 540
cggtggacag gtgaacttgg atatggagga ccatcgggac gaggactttg tgaagcccaa 600
aggagccttc aaagccttca ctggcgaggg tcagaaactg ggcagcactg cccccaggtg 660
ttgagtacca gctctccagc ccaacaggca gaaaatgaag ccaaagccag ctcttccatc 720
ttaatcgacg aatcagagcc taccacaaac atccaaattc ggcttgcaga cggcgggagg 780
ctggtgcaga aatttaacca cagccacagg atcagcgaca tccgactctt catcgtggat 840
gcccggccag ccatggntgc caccagcttt atcctcatga ctactttccc gaacaaagag 900
ctggctgatg agagccagac cctgaaggaa gccaacctgc tcaatgctgt catcgtgcag 960
cggttaacat aaccgcccag ccagctgcct ggcctccctc ctgtgtttcc catggccagt 1020
ggccatgccc catgggggatc gcccctcctg ccccttgtg cacacccagc agtccagtgc 1080
aacgtctcct ccatagctct gggttcttag atcttggttg gacgtttgtt ttctccttag 1140
ttgcatttcc tgggtttttg tgatgatcaa tggactttaa tgaaaaaaaa aataaaaaca 1200
accnaaaggg gggcccggtc ccaatncccc cctt 1234

<210> 128
<211> 863
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (840)
<223> n equals a,t,g, or c

<400> 128
cccacgcgtc cgcaggcgcg ctcgggctgc cgctggctct tcgcacgcgg ccatggccga 60
ctccgagctg cagctggttg agcagcggat ccgcagcttc cccgacttcc ccaccccagg 120
cgtggtattc agggacatct cgcccgtcct gaaggacccc gcctccttcc gcgccgccat 180
cggcctcctg gcgcgacacc tgaaggcgac ccacgggggc cgcatcgact acatcgcagg 240
cctagactcc cgaggcttcc tctttggccc ctccctggcc caggagcttg gactgggctg 300
cgtgctcatc cgaaagcggg ggaagctgcc aggccccact ctgtgggcct cctattccct 360
ggagtacggg aaggctgagc tggagattca gaaagacgcc ctggagccag gacagagggt 420
ggtcgtcgtg gatgatctgc tggccactgg tggaaccatg aacgctgcct gtgagctgct 480
gggccgcctg cargctgagg tcctggagtg cgtgagcctg gtggagctga cctcgcttaa 540
gggcagggag aagctggcac ctgtaccctt cttctctctc ctgcagtatg agtgaccaca 600
gggcctccca gcccaacatc tccagctgga tcccagggaa atatcagcct tgggcaactg 660
cagtgaccag gggcaccggc tgcccacagg gaacacattc ctttgctggg gttcagcgcc 720
tctcctgggg ctggaagtgc caaagcctgg ggcaaagctg tgtttcagcc acactgaacc 780

caattacaca cagcgggaga acgcagtaaa cagctttccc acaaaaaaaa aaaaaaaaan 840
aaaaaaaaaa aaaaagggcg gcc 863

<210> 129
<211> 1238
<212> DNA
<213> Homo sapiens

<400> 129
cacagtgtct gctgtgattg agatgcgcac aggttggggg aggtagggcc ttacgcttgt 60
cctcagtggg ggcagtttgc cttagatgac arctgggctc ttcttcacac cacctgcagc 120
ccctccctgc ccctgcccta gctgctgtgt gttcagttgc cttctttcta cctcagccgg 180
cgtggagtgg tctctgtgca gttagtgcca ccccacacac ccgtctcttg attgagatgt 240
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gctggcgctc tccctcagca caggtgggtc agtggccagc aggcccatct ggagtgggag 360
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tcccgggtga ctggcagttt tcacggtcta gggccgagac gatggcatgg ggcctagagc 480
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cccaggtact tgagttttgg aaaagctgac tcacgcccat ccatctcaca gcccttccct 720
ggggacagtc gcttccgcct tgacacctca ctctcagttg aataactcaa gcttggtcat 780
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tctgtcctgt tggctgcttg cttccagctc cccccaatct ccatcgcagc gggttcctcc 1140
tgtcttttct acagtgtcat aaaacatcct gcccctaccc tctcccaaag gtcaatttta 1200
attctyawca agaagattta tgaggagaag aaaaagaa 1238

<210> 130
<211> 379
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (373)
<223> n equals a,t,g, or c

<400> 130
tggtttggga gctgccaggc tcctgggagg atcgcagtca gcagagcagg gctgaggcct 60
gggggtagga gcagagcctg cscatctgga ggcagcatgt ccaagaaagg gagtggaggt 120
gcagcraagg acccaggggc agagccacgc tggggatgga ccccttcgag gacacgctgc 180
ggyggctgcg tgaggccttc aactgakggc gcacgcggcc ggccgagttc cgggctgcgc 240
actccagggc ctgggccact tccttcaaga aaacaagcar cttctrcgmg acgtgctggc 300
ccaggaactg cataagccag ctttcgaagg cagacatatc tgagtcatcc tttgccagaa 360
cgaggttgaa tangctctt 379

<210> 131

<211> 1786
<212> DNA
<213> Homo sapiens

<400> 131
cctgggcgct aagatggcgg cggcgtgagt tgcatgttgt gtgaggatcc cggggccgcc 60
gcgtcgctcg ggccccgcca tggccgtcac catcacgctc aaaacgctgc agcagcagac 120
cttcaagatc cgcatggagc ctgacgagac ggtgaaggtg ctaaaggaga agatagaagc 180
tgagaagggt cgtgatgcct tccccgtggc tggacagaaa ctcatctatg ccggcaagat 240
cttgagtgac gatgtcccta tcagggacta tcgcatcgat gagaagaact ttgtggtcgt 300
catggtgacc aagaccaaag ccggccaggg tacctcagca cccccagagg cctcacccac 360
agctgcccca gagtcctcta catccttccc gcctgccccc acctcaggca tgtcccatcc 420
cccacctgcc gccagagagg acaagagccc atcagaggaa tccgccccca cgacgtcccc 480
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ctccacgcta gtgacgggct ctgagtatga gacgatgctg acggagatca tgtccatggg 600
ctatgagcga gagcgggtcg tggccgccct gagagccagc tacaacaacc cccaccgagc 660
cgtggagtat ctgctcacgg gaattcctgg gagccccgag ccggaacacg gttctgtcca 720
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gcgggaccag ccccagttcc agaacatgcg gcaggtgatt cagcagaacc ctgcgctgct 840
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gcaccaggag cagttcatcc agatgctgaa cgagcccccct ggggagctgg cggacatctc 960
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cctggtcatc caggcctatt tcgcgtgtga aaaaaatgag aacttggctg ccaacttcct 1140
cctgagtcag aactttgatg acgagtgatg ccaggaagcc aggccaccga agcccccacc 1200
ctacccttat tccatgaaag ttttataaaa gaaaaaatat atatatattc atgtttattt 1260
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caactttgat cctccattgg agtggcccaa atctttccat ctagggcaag tcctgaaagc 1620
ccaaggcccc ctccccagtc tggccttgcc tccagcctgg agaagggcta acatcagctc 1680
attgtcaagg ccaccccccac cccagaacag aaccgtgtct ctgataaagg ttttgaagtg 1740
aataaagttt taaaaactaa aaaaaaaaaa aaaaaaaaaa aaaaaa 1786

<210> 132
<211> 974
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (165)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (853)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (963)
<223> n equals a,t,g, or c

<400> 132
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cgagtcggac cctgatgctt ggtgtgacct gagtaaattt gacctccctg aggaaccatc 120
tgcagaggac agtatcaaca acagcctagt gcagctgcaa gcgtncacat cagcagcaag 180
tcctgccacc ccgccagcct tccgccctgg tgcccagtgt gaccgagtac cgcctggatg 240
gccacaccat ctcagacctg agccggagca gccggggcga gctgatcccc atctccccca 300
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cctgtaacag cctcacgccc aagagcacac ctgttaagac cctgcccttc tcgccctccc 480
agtttctgaa cttctggaac aaacaggaca cattggagct ggagagcccc tcgctgacat 540
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ccctgcacca gaaacatgct gcgtttgtaa ccccagatca gaagtactcc atggacaaca 660
ctccccacac gccaaccccg ttcaagaacg ccctggagaa gtacggaccc ctgaagcccc 720
tgccacagac cccgcacctg gaggaggact tgaaggaggt gctgcgttct gaggctggca 780
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aanttttcca gcct 974

<210> 133
<211> 634
<212> DNA
<213> Homo sapiens

<400> 133
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cttagagaag aaccctgaaa tcagaccagt ttttgcggcc tccccctttc ctctctgtta 120
cagtgccctt tccaggcctt aagagaagta aaacttagct gcagcgtcag gaggtggacc 180
ccagagtgtg agtggcacgc ttctctgtga acccgtcctc accatgtttg ccacatctgg 240
ggcagtggca gcggggaagc cttactcgtg cagcgaatgt ggcaagagct tctgctacag 300
ctcagtgctg ctgcgacatg aacgagctca cggcggtgac ggccgcttcc gttgcctaga 360
atgcggtgag cgctgtgcac gggctgctga cctccgagcg cacaggcgca cgcatgctgg 420
ccagaccctc tacatctgca gtgagtgcgg acaaagcttc cgccacagcg gccgtcttga 480
cctacacttg ggcgcacacc ggcagcgatg ccgcacttgc ccctgccgca cwtgcggccg 540
gcgcttcccg cacctcccgg cgctgctgct acaccggcgc cgccagcatc tgccagagcg 600
gccccgscgy tgcccgctgt gcgycctcag gttt 634

<210> 134
<211> 1855
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1818)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1845)
<223> n equals a,t,g, or c

<400> 134
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ggcgaggggc tgcagtgcgt ggtgcccttc ggggtgccag cctcggccac ggtgcggcgg 120
cgcgcgcagg ccggcctctg tgtgtgcgcc acagcgagcc ggtgtgcggc agcgacgcca 180
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ggccgccggt catcgtcctg cagcgcggag cctgcggcca agggcaggaa gatcccaaca 300
gtttgcgcca taaatataac tttatcgcgg acgtggtgga gaagatcgcc cctgccgtgg 360
ttcatatcga attgtttcgc aagcttccgt ttctaaacgg agaggtgccg gtggctagtg 420
ggtctgggtt tattgtgtcg gaagatggac tgatcgtgac aaatgcccac gtggtgacca 480
acaagcaccg ggtcaaagtt gagctgaaga acggtgccac ttacgaagcc aaaatcaagg 540
atgtggatga gaaagcagac atcgcactca tcaaaattga ccaccagggc aagctgcctg 600
tcctgctgct tggccgctcc tcagagctgc ggccgggaga gttcgtggtc gccatcggaa 660
gcccgttttc ccttcaaaac acagtcacca ccgggatcgt gagcaccacc cagcgaggcg 720
gcaaagagct ggggctccgc aactcagaca tggactacat ccagaccgac gccatcatca 780
actatggaaa ctcgggaggc ccgttagtaa acctggacgg tgaagtgatt ggaattaaca 840
ctttgaaagt gacagctgga atctcctttg caatcccatc tgataagatt aaaaagttcc 900
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<210> 135
<211> 917
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (913)
<223> n equals a,t,g, or c

<400> 135
ggtttttgc gcgtgcatat ggcggtggcg ggtgggggga agggggagat cctgctgcac 60

tggccgccca agttgggggg cgagctcggt ggtgacgcgc ggccctcacg tgacccarag 120
ctgcagagcg acgcagcctt cggtgcagtc gtcactcgcg tctggctacc agctccccgc 180
tgccctgagc tcggcgggct ggcattcggc ccggggaaaa gcggagcagg tctgcgaggc 240
taagtgtctc cgcggcgcac ctcgcggcga gaatccggag gagaaggaga ctgcaaggat 300
aggcccagga aaacgaagag atggagcagc ctatgcagaa tggagaggaa gaccgcccctt 360
tgggaggagg tgaaggccac cagcctgcag gaaatcgacg gggacaggct cgccgacttg 420
cccctaattt tcgatgggcc atacccaata ggcagatcaa tgatgggatg ggtggagatg 480
gagatgatat ggaaatattc atggaggaga tgagagaaat cagaagaaaa cttagggagc 540
tgcagttgag gaattgtctg cgtatcctta tgggggagct ctctaatcac catgaccatc 600
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tcccgctgtt ttctttttcc ttgcattttc ctaatatgcc tttactgatc cgtttgctgt 720
gaaccctatg ttatttccat gtgtcaagtg ggtcttgtgt tgccagcttc tatttgaaga 780
ttgcctttgc actcagtgta agtttctgtc agcagtagtt tcacccattt gcatggaaaa 840
atttaaagct aataaagcaa tttaaaaagc aaaaaaaaaa aaaaaaaaaa aaaaaamamg 900
gggggcccg gwnccca 917

<210> 136
<211> 1271
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1236)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1255)
<223> n equals a,t,g, or c

<400> 136
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ggcctgtctg cagaatccac ascaaccagc accatgccca tgayactggg gtactggrac 120
atccgcgggc tggcccaykc catccgcctg ctcctggaat acacagactc aagctaygag 180
gaaaagaagt acacgatggg ggacgctcct gattatgaca gaagccagtg gctgaatgaa 240
aaattcaagc tgggcctgga ctttcccaat ctgccctact tgattgatgg grctcacaag 300
atcacccaga gcaacgccat cctgcggtac attgcccgca agcacaacct gtgcggggaa 360
tcagaaaagg agcagattcg cgaagacatt ttggagaacc agtttatgga cagccgtatg 420
cagctggcca aactctgcta tgacccagat tttgagaaac tgaaaccaga atacctgcag 480
gcactccctg aaatgctgaa gctctactca cagtttctgg ggaagcagcc atggtttctt 540
ggggacaaga tcacctttgt ggatttcatc gcttatgatg tccttgagag aaaccaagta 600
tttgagccca gctgcctgga tgccttccca aacctgaagg acttcatctc ccgatttgag 660
ggcttggaga agatctctgc ctacatgaag tccagccgct tcctcccaag acctgtgttc 720
acaaagatgg ctgtctgggg caacaagtag ggccttgaag gccaggaggt gggagtgagg 780
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tcagccccga gctgtccccg tgttgcatga aggagcagca ttgactggtt tacaggccct 1140

gctcctgcag catggtccct gccttaggcc tacctgatgg aagtaaagcc tcaaccacaa 1200
aaaaaaaaaa aaaaaatttg gggggggcc cgttanccca tttggccctt taggnggggg 1260
ggttttaaat t 1271

<210> 137
<211> 2017
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (295)
<223> n equals a,t,g, or c

<400> 137
ggaatgtcat cagtgttgac ccgaatgatc agaaaaagac agcttgttat gacattgatg 60
ttgaagtgga tgacaccttg aagacccaga tgaattcttt tctgctgtcc actgccagcc 120
aacaggagat tgctactcta gacaacaaga caatgactga tgtggtgggt aaccorarga 180
rgagcgccga gctgagttct acttccagcc ctgggkcagg aggctgtgtg ccratacttc 240
tactccaagg tgcagcagag acgacaagaa ttagagcaag ccctgggaat ccggnataca 300
tagggcctct cccacagccc tgattcgact gcaccaattc ttgawttggg ccctgtgctg 360
cctgcctcat agtatctgcc ttggtcttgc ttggggcgtt ccaggggatg ctgttggttc 420
aaggacaaca ccagaatgaa gagggtctca caagacacct gttatcctct tctttcaccc 480
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ccctggtcta catagaacct ctagatagtg ttagagagag aacatgtagt ggtaatgagt 600
gcttggaatg gattgggcct caggccaggt ggtcttcaag gggaccagct aactgatcct 660
gcccttcaga gacccaggag ttgggagctt tcgctccttc tccaagactc aggcctgtgg 720
gcactctata agctagttga tcttggctct cctgataaca gaatccaatt tccttccttc 780
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acaaaggggg aattccgttc agcatgggct ctaaacccac agaactgaca aagcccctgc 1620
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ccatgagaag gaagctcagt acttcccaca gtgtccctgt tgataactgt ttttattaac 1860
tgaattgttt ttttcatgga ccaaactttt ttttgtactg tccccttatt gatgttaccc 1920
agttttaata aaagaatctt ctgaaggatg ggtcctccta cctactgtga gagagctctt 1980
ccctgagctc ttcttccttc aataccatta aaaaaaa 2017

<210> 138

<211> 937
<212> DNA
<213> Homo sapiens

<400> 138
gattcaaaca ggcaacaatg accttttatt ttctgtttgt ccccacctcc ccagccttcc 60
acctcctgtt cttcctacct tcttcctttt tgactaaata atccccacct cccttgatca 120
tacagtgagg ctacagtgac tgaggggaga atccctcctg ttcactctcc caaccctgct 180
ccagcccctc agcttcccag accctcatgc agttggttgt aaattctccc aggagctgtt 240
ttactgtcta cttttcagga ttaaaaaaaa aatcaaaact taaaaaaaaa aaagtttaaa 300
aagcaaaatg gggaggggga ggaagcagtg actttttttt ggtaattatg cgcttttttt 360
taatttttag aatttgtctt tttactgtgg gtgggctgtt gatatttcat caagataagc 420
atttctttcc tgagttcagg tgactgagga agagccacaa aacaaaacac aacaaaacca 480
aaccacagaa tcatctttaa cccaactttt tatacgatgc cccagttccc cataactttg 540
cacacaagct tctgtgttca gttgaattgt aactgctttt tgtatttgga gagagtgact 600
attgaacttg aaacctttta ttccgggcgt cttggtagtt tctggtggga ttcagtgggt 660
gagagggaag aaggggaggt tggggggctc cttcccttca gaacttgaag tttctcccac 720
tgcctcctct ccagtggtct cccaggtgcc agacccaaaa gcttttccta cagtgatacc 780
ctttattttt acttcccctt gactcatatg ttttaacatg attttaacaa actgcactta 840
ttaagaaatg tgtttgccct gttttgtttg gtttcgtttt gttttctttg aataaatgac 900
atggcacctc ctagcaggaa ggaaaaaaaa aaaaaaa 937

<210> 139
<211> 2759
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (171)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1654)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2743)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2744)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2746)
<223> n equals a,t,g, or c

<400> 139
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cgttggaact accgggacga ggctgatgtg ctggaagtgg atcagggctt tgatgatcac 120
aacctgccct gtgatgtcat ctggctagac attgaacatg ctgatggcaa ncggtatttc 180
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cacgaggagc tgcggaacct ggggctgtat gtwaaaaccc gggatggctc tractatrag 360
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gcccagcatt atgggggctg ggagcaccgg gatgtgcata acatctatgg cctttatgtg 600
cacatggcga ctgctgatgg gctgagacag cgctctgggg gcatggaacg cccctttgtc 660
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gctagtctaa gacccagatt ctgccaacat ttgggcagga tgagaggggct gaccctgggc 1860
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tggggagtcg gggaatattt gtgggtattt tttttacttc ctcttggttc ccagctgtga 2640
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aannanaaaa aaaaataaa 2759

<210> 140
<211> 1241

<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (317)
<223> n equals a,t,g, or c

<400> 140
tcgacccacg cgtccgggag aacgggcgga gggcgcgggc cgaccgggcg caccgaccat 60
ggcctccaaa tgccccaagt gcgacaagac cgtgtacttc gccgagaagg tgagctccct 120
ggggaaggac tggcacaagt tctgcctcaa gtgcgagcgc tgcagcaaga cgctgacgcc 180
cgggggccac gccgagcatg acgggaagcc gttctgccac aagccgtgct acgccaccct 240
gttcggaccc aaaggcgtga acatcggggg cgcgggctcc tacatctacg agaagcccct 300
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gaaggcgagc ggccccccga aggscccagc agagcctcca gtgtcaccac tttcaccggg 420
gagcccaaca cgtgcccgcg ctgcagcaag aaggtgtact tcgctgagaa ggtgacgtct 480
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cccggcgggc acgcggagca cgacggccag ccctactgcc acaagccctg ctatggaatc 600
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<211> 3405
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<213> Homo sapiens

<220>
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<222> (1569)
<223> n equals a,t,g, or c

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<211> 2268

<212> DNA
<213> Homo sapiens

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<222> (2169)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2196)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2232)
<223> n equals a,t,g, or c

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<211> 1757
<212> DNA
<213> Homo sapiens

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<211> 1062
<212> DNA
<213> Homo sapiens

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<221> misc feature

<222> (52)
<223> n equals a,t,g, or c

<220>
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<222> (1056)
<223> n equals a,t,g, or c

<400> 144
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<210> 145
<211> 1030
<212> DNA
<213> Homo sapiens

<400> 145
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<213> Homo sapiens

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<210> 147
<211> 2678
<212> DNA
<213> Homo sapiens

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ttcctcattt tgaattatgt gcactaccat agctacatca gtttgataca gtattgaaaa 2400
attatcagtt atattttgcy gtttatgrtc tatttgtagr ttaggrttaa aatggrttta 2460
atccattttt aaggstgtgt gaatttttct aaacaagaac catttgcaat atggatttct 2520
tagagattaa accaattata acttattagc agtsgcgagc acatgttcat atagtcaatg 2580
taaaaataca ctaatgagta tttggtaaat cccagtaggc ttttaccatt agcataattt 2640
tgtgttgtac ctcggccgcg accacgctaa gccgaatt 2678

<210> 148
<211> 1028
<212> DNA
<213> Homo sapiens

<400> 148
ctgcctcagc ctcccgagta gctgggatta caggcacaca ccaccacgcc cggctaattt 60
tttgtgtctt tttagtagag acggggtttc gctatgttgg ccagactggt cttgaactgc 120
tgacctcgtg atccgcccgc ctcggcctct caaagtgctg ggattctgtg tgttttgtgc 180
acctccactt taggtaatca tagggagcac atttacagga tggtctaata acatgaaaac 240
aggctagttt caagcaacag caatgtcggt tggaaagcag gcgtcatttg ccttgaaaaa 300
agccttttga caacatacag gcattctttt aaaaccaggc tgaaacattt tatttccgag 360
acttaacgtt gtgtttcctg tttcttaaac ctagcacctc tgtgtatttg aaaataatga 420
gacatctttc attggatttt ggaaaattgt tccccatggg attctaacct cactaccaaa 480
tgagtgaaag cttgattaag agttcttcca tatactagcc tccttggaag aagtgatcag 540
aaggtgataa gaaggacaga aaggactatt ttaaagttgg actgaaggag aaaaaagcaa 600
aattcttgtt tcatcccaat tctagttaga acaaagttaa acccccgtaa tcttaaagag 660
aaaatctttg gaggttttaa ttaaacattt tatacattta aagtcttgtt aatggtgctt 720
taagtgtcaa tgtagcatgt aaaaggcttt gtacagacag gtaaaagttc catttctgag 780
tgatgaaatg taacacttct tcatctttaa cttgaaatca aaactatcag attttatttt 840
tgtataattt aaggaaggta aagttagggg actagaagac tctaaattgg cttctacaga 900
tcaataattt aaatgtaact agttgggatt ttatagttaa aattatattt gtgtatataa 960
cataactaat ctgtaaattg taataaatat atttgcaatt attaaatgtt aagtgatatt 1020
ttggttca 1028

<210> 149
<211> 1425

<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (647)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1359)
<223> n equals a,t,g, or c

<400> 149
gcgtctccgg aagtggaggc gggagcggca cggcagccac tgcttggggt agcgggaggg 60
cagactctgg gcgccactcc cgggccggtc atgaacgggc cggcggacgg cgaagtggac 120
tacaaaaaaa aataccggaa tctgaagcgg aagctcaagt tcctcatcta cgagcacgag 180
tgcttccagg aggagctgag gaaagcgcaa aggaaattac tgaaggtgtc ccgggacaag 240
agtttcctcc tagaccgact tctgcagtac gagaacgtgg atgaagactc ttcggactca 300
gatgccactg catcatcaga taacagcgag acggagggga cacccaagtt gtctgacaca 360
ccggccccta agaggaagag aagccctccg ctgggggcg ccccctctcc ctccagcctc 420
tccctgcctc cttcaacagg gtttcccctt caggcctccg gggtcccctc cccatacctg 480
agctcgctgg cctcctcccg ctacccccca ttcccttctg actacctggc cctgcagctg 540
cccgascccca gtcccctrag gcccaagcgg gagaaacggc cccgmctgcc ccggaaactc 600
aagatggcgg tgggaccccc cgaytgccct gtgggagggc cgctganctt ccctggccgg 660
ggttytgggg stggggtcgg gamaaccctg amcccccttc cacccccctaa gatgcccccc 720
cccacgatcc tgagcacggt ccctcggcag atgttcagcg atgcaggtag cggggacgat 780
gccttggatg gagacgatga cctggtgatc gacatcccgg agtgaccgtg acatcacgcc 840
atgcccacca cggccccgcc cggcgccctc cccgtgccag cacacacgag tccagcttcc 900
tcggaggtgt ttattgatgc ccagctgcca tgctccggcc actgacacaa ccagaaaagg 960
cgtaaacatg cacgggtgtc ccccaggagg gtgcaggggc cctgccttca aaccccgggc 1020
ccctccaggg gacagttatt taaacgagtg gccgggagca tctgccacct gctggggagg 1080
cagagaccct gcaatggcca cctctttaaa agggcagctg tacagggcta ggtttttca 1140
atgaagtttc tgtattaaag gagtggctct gggtttgttt tttgtccttt ttttttgaga 1200
cattctcctc ctctgaacct cccctaatcc gacctcctcc ctgttggggg agagggacgg 1260
ggcagcgtgg agaggcagga gtgaggagcg cgggggcctg gggccgggct ctgagcactg 1320
cccgggtgtg cagatgatgg ggggtttgca tatttgcang ggactagcga gtcaggcagg 1380
aggtttgcat atgtgaatat agaactccgc agcccctcat gagca 1425

<210> 150
<211> 780
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (285)
<223> n equals a,t,g, or c

<400> 150
gctgcgagaa gacgacagaa ggggagagcc aatggaaagg ggctgccgcg cggccgtaaa 60

gagtttgtag agcagttcgg gtgcggtacg ttgcattccg gtaccggacg ccgagagcgg 120
tttgtctccg tctctggagt tgtaggcgag aggtgatcat gtccggtcgc gggaaacagg 180
gcggcaaagt gcgagcaaag gccaaatccc gctcctcccg cgcgggcctg cagttcccgg 240
tgggccgagt gcacagactg ctgcgcaaag ggaactacgc ggasnagtgg gcgccggggc 300
gccggtgtac ctggcggcgg tgttggagta ccttacggcg gagatcctgg agctggctgg 360
caacgccgcg cgtgacaaca agaagaccag gataattccc cgccacctgc agctcgccat 420
ccgcaacgac gaggagttaa acaagctgct gggcaaagtg accatcgctc agggcggcgt 480
cctgcccaac atccaggccg tgctgctgcc caagaagacg gagagtcaga agacgaagag 540
caaatgaccc tgacgccgcc ctcagggagc tggctccscc agcaaaggcc cttttcatgg 600
tcgtcccgca atgcttttga atgtgctgga tgtcatggag ggccggtgac atctagcggg 660
gaggtgggcg gcgagggtcc cggcgggagc caataaagtt ggtgaaaatc gtaaaaaaaa 720
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780

<210> 151
<211> 1066
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1061)
<223> n equals a,t,g, or c

<400> 151
ggacccgcca tggcgcggaa gaaggtgcgt ccgcggctga tcgcggagct ggcccgccgc 60
gtgcgcgccc tgcgggagca actgaacagg ccgcgcgact cccagctcta cgcggtggac 120
tacgagacct tgacgcggcc gttctctgga cgccggctgc cggtccgggc ctgggccgac 180
gtgcgccgcg agagccgcct cttgcagctg ctcggccgcc tcccgctctt cggcctgggc 240
cgcctggtca cgcgcaagtc ctggctgtgg cagcacgacg agccgtgcta ctggcgcctc 300
acgcgggtgc ggcccgacta cacggcgcag aacttggacc acgggaaggc ctggggcatc 360
ctgaccttca aagacgcctc tttttcttca tcagggaaga ctgagagcga aggcgcggga 420
gatcgaacac gtcatgtacc atgactggcg gctggtgccc aagcacgagg aggaggcctt 480
caccgcgttc acgccggcgc cggaagacag cctggcctcc gtgccgtacc cgcctctcct 540
ccgggccatg attatcgcag aacgacagaa aaatggagac acaagcaccg aggagcccat 600
gctgaatgtg cagaggatac gcatggaacc ctgggattac cctgcaaaac aggaagacaa 660
aggaagggcc aagggcaccc ccgtctagaa tgccagaacc agcgggtggc cttaggggct 720
gtgaggcagt ggggacctta ttgatgaaag aaaccgtctt tgcgttacac ccgagtctgc 780
ctctcggagc agggagctca ccttccgcga cgtgttctga gggtctgcat cttagggggg 840
agggctgggg caaatcgcca cctgtgcctt tcctctggcc ctgctgcccc cacacccaac 900
tccgagggcc cacgctgggg aaagcgggaa gcgctcgctc cctttccccc attagtgctc 960
tctctgcctg gatcccggca gaagctatga aagggaataa agagaaaaga artamaaaaa 1020
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa nccccct 1066

<210> 152
<211> 1649
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1543)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1579)
<223> n equals a,t,g, or c

<400> 152
accccggctc tccaaggagg tgtgacatca tcatcatctc tggccggaaa gaaaagtgtg 60
aggctgccaa ggaagctctg gaggcattgg ttcctgtcac cattgaagta gaggtgccct 120
ttgaccttca ccgttacgtt attgggcaga aaggaagtgg gatccgcaag atgatggatg 180
agtttgaggt gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca 240
cgggcctcgc tgcaaatttg gaccgggcca aggctggact gctggagcgt gtgaaggagc 300
tacaggccga gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc 360
ccaaatacca tcccaagatt atcgggagaa agggggcagt aattacccaa atccggttgg 420
agcatgacgt gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa 480
ttaccatcac agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg 540
tgggtgaact tgagcagatg gtttctgagg acgtcccgct ggaccaccgc gttcacgccc 600
gcatcattgg tgcccgcggc aaagccattc gcaaaatcat ggacgaattc aaggtggaca 660
ttcgcttccc acagagcgga gccccagacc ccaactgcgt cactgtgacg gggctcccag 720
agaatgtgga ggaagccatc gaccacatcc tcaatctgga ggaggaatac ctagctgacg 780
tggtggacag tgaggcgctg caggtataca tgaaaccccc agcacacgaa gaggccaagg 840
caccttccag aggctttgtg gtgcgggacg caccctggac cgccagcagc agtgagaagg 900
ctcctgacat gagcagctct gaggaatttc ccagctttgg ggctcaggtg gctcccaaga 960
ccctcccttg gggccccaaa cgataatgat caaaaagaac agaaccctct ccagcctgct 1020
gacccaaacc caaccacaca atggtttgtc tcaatctgac ccagcggctg gaccctccgt 1080
aaattgttga cgctcttccc ccttcccgag gtccgcaggg agcctagcgc ctggctgtgt 1140
gtgcggccgc tcctccaggc ctggccgtgc ccgctcagga cctgctccac tgtttaacac 1200
taaaccaagg tcatgagcat tcgtgctaag ataacagact ccagctcctg gtccacccgg 1260
catgtcagtc agcactctgg ccttcatcac gagagctccg cagccgtggc taggattcca 1320
cttcctgtgt catgacctca ggaaataaac gtccttgact ttataaaagc caaacgtttg 1380
ccctcttcct ttcccacctc cctcctgcca gtttcccttg gtccagacag tcctgtttgt 1440
ggagtgcaat cagcctcctc cagctgccag agcgcctcag cacaggtgtc agggtgcaag 1500
gaagacctgg caatggacag caggaggcag gttcctggag ctngggggtg acctgagagg 1560
cagagggtga cgggttctna ggcagtcctg attttacctg ccgtggggtc tgaaarcacc 1620
aagggtccct gaccctacct ccactgcca 1649

<210> 153
<211> 660
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (35)
<223> n equals a,t,g, or c

<400> 153
ccggaaattc ccgggtcgac ccacgcgkcc gcggnagwgc tcacacgtgt gctccctgcc 60
ctgctcctgg ccccttggcc ggccgggctg tttctggcca tgggtcgctc ccgccggaca 120
ggcgcgcacc gagcgcactc tctagcccgg cagatgaagg cgaacggcgg cggccggact 180

tggatgagat tcaccgcgag ctgcggcctc agggatccgc acgaccccag cccgacccaa 240
acgccgagtt cgaccccgac ctgccagggg gcggtctgca ccgctgtctg gcctgcgcga 300
ggtacttcat cgattccacc aacctgaaga cccacttccg atccaaagac cacaagaaaa 360
ggctgaagca gctgagcgtc gagccctaca gtcaggaaga ggcggagagg gcagcgggta 420
tgggatccta tgtgcccccc aggcggctgg cagtgcccac ggaagtgtcc actgaggtcc 480
ctgagatgga tacctctacc tgacatggcc tgaagatgca gggcagagga attgcccatg 540
gacagtgacg caaggactag gctgggaggg agcgtgccaa ccccttttgc ctctgggttt 600
ggggagcgga gggcctcttc ttggtgccct gcccccaata aaggaactgg acaaagagaa 660

<210> 154
<211> 605
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (449)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (574)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (578)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (583)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (587)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (596)
<223> n equals a,t,g, or c

<400> 154
ggcagagctc caccttccat ccggcgccgg ctttcggcgc gacggtcgcc gcgttccatc 60
gtcgcgcggc ccttcgggcg cccgagcccg caatgtcggg ccccaacgga gacctgggga 120
tgccggtgga ggcgggagcg gaaggcgagg aggacggctt cggggaagca gaatacgctg 180
ccatcaactc catgctggac cagatcaact cctgtctgga ccacctggag gagaagaatg 240
accacctcca cgcccgcctc caggagctgc tggagtccaa ccggcagaca cgcctggagt 300
tccagcagca gctcggggag gcccccagtg atgccagccc ctaggctcca agagcccccca 360

accgggaccc aaccctgcct ccctgggcta ggctctggcc tgggcactca mcccctggct 420
tagacamctt ctcaagggct ggccttcang gacccctggt gggtctgcct gcctgggcca 480
accttcctgc ctgggsctyc ccttggctam ctgggscagc cccaccaac tggcatgccc 540
tcctgggggc caaagaatgg ggcctgcaac ccanccantt gcntgcncaa cccaanttcc 600
tgggg 605

<210> 155
<211> 695
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (173)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (499)
<223> n equals a,t,g, or c

<400> 155
gaaccctaga aaaaaggatg cagtactaaa gtgtcattca ttcaaagcca ctcctctttt 60
ggtattccac ccattttcca gacggtgaca ctgaggctca ggaagcagta gggacttgca 120
caaagccctt tgggaagcag gctgggaaac agtggaggga gggtgtccat tanccccaag 180
gagacacagg atctgggctc tktytttsgc cttcctccca gaatacgctg ccatcaactc 240
catgctggac cagatcaact cctgtytgga ccacctggag gagaagaatg accacctcca 300
cgcccgcctc caggagctgc tggagtccaa ccggcagaca cgcctggagt tccagcagca 360
gctcggggag gcccccagtg atgccagccc ctaggctcca agagccccca accgggaccc 420
aaccctgcct ccctgggcta ggctctggcc tgggcactca cccccctggct tagacacctt 480
ctcaagggct ggccttcang gacccctggt gggtctgcct gcytgggcca cccttcctgc 540
ctgggrcctc cccttggkcc tactggggcc agcccccacc acctggcatg ccctcctggg 600
gccaagagtg ggcctgcaam ccacccattg sctgcccaac caattcctgg gcgytcccca 660
wtytgcccag gcttgaatgt tcacatgaaa tgggt 695

<210> 156
<211> 780
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (289)
<223> n equals a,t,g, or c

<400> 156
cggtgggctc gcgttgaggc tgcggtcatg gagggagcag gagctggatc cggcttccgg 60
aaggagctgg tgagcaggct gctgcacctg cacttcaagg atgacaagac caaagtgagc 120
ggggacgcgc tgcagctcat ggtggagttg ctgaaggtct tcgttgtgga agcagcagtc 180
cgcggcgtgc ggcaggccca ggcagaagac gcgctccgtg tggacgtgga ccagctggag 240
aaggtgcttc gcagctgctc tggacttcta gggatctcag ccgtggckna ggccaccccc 300

agaggagccc ctggtccaca gaagcaggcc ttgtgtttcc agcggcctct gataagaggc 360
agggaaggam ctgaaggatt tggarttgat tcaaacaaga tctctgggag tctccagcct 420
gtgcagaagg ggcaggactg cagtgcactg cgggccttgg agtgtccagt ggggacactg 480
gtgtgggaag gggcagcacc tggggagtcc ctgcctctcc tccctgggac aatagtgtgc 540
atgccacccg gggtcctaca ggcaggtgct gggaaaggcc tggccagcag gtagcctgtg 600
tgtttgacaa acagcagctg gcagcgctgc ctcctgccca cattcctgcc acccgacatc 660
aaagctggcg tgtgaccttt ccagccatgc gatattcccc ttggaagatg cttccccagg 720
ctataaattt gttctcacaa agcaacatca ataaatcaaa actgtctcty ccaaaaaaaa 780

<210> 157
<211> 1127
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1113)
<223> n equals a,t,g, or c

<400> 157
aacttcagtg ccctcactgt agaatttaaa agccttactg ttgattgccc atggtggact 60
tgatggagaa attaaatatc tttcattatg ctttacaaaa tactgtatat gtttcagcaa 120
gtttggggaa tgggagagga caaaaaaaag ttacatttaa tctatgcatt tttgccaagc 180
catattgagt tattttacta ctagagacat taggaaacta actgtacaaa agaaccaagt 240
ttaaaagcat tttgtggggt acatcatttc tataattgta taatgtattt ctttgtggtt 300
ttaaatgata aagacattaa gttaacaaac atataagaaa tgtatgcact gtttgaaatg 360
taaattattc ttagaacact ttcaatgggg gttgcattgt ccttttagtg ccttaatttg 420
agataattat tttactgcca tgagtaagta tagaaatttc aaaaaatgta ttttcaaaaa 480
attatgtgtg tcagtgagtt tttcattgat aattggttta atttaaaata tttagaggtt 540
tgttggactt tcataaattg agtacaatct ttgcatcaaa ctacctgcta caataatgac 600
tttataaaac tgcaaaaaat gtagaaggtt gcaccaacat aaaaaggaaa tatggcaata 660
catccatgat gttttccagt taacatagga attaccagat aaatactgtt aaactcttgt 720
ccagtaacaa gagttgattc atatggacag tatgatttat tgtttatttt tttaaccaaa 780
tacctcctca gtaatttata atggctttgc agtaatgtgt atcagataag aagcactgga 840
aaaccgatcg tctctaggat gatatgcatg tttcaagtgg tattgaaagc cgcactgatg 900
gatatgtaat aataaacata tctgttatta atatactaat gactctgtgc tcatttaatg 960
agaaataaaa gtaatttatg gatgggtatc tttaattttt actgcaatgt gttttctcat 1020
ggctgaaatg aatggaaaac atacttyaat tagtctctga ttgtatataa atgtttgtga 1080
aattccatgg ttagattaaa gtgtrttggg aanaattctc catgggg 1127

<210> 158
<211> 1282
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (120)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (205)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (207)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (236)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (732)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1279)
<223> n equals a,t,g, or c

<400> 158
tgctctacaa atagtaaaaa taaaaaataa aaaaagtagc tgggcgtggt ggtgtgcacc 60
tgtggtccca gctgcttggg atgctgaggt ggaaggatct cttaaaccca ggagggtggn 120
aggctgcagt gaacttgcga ttgcaccact ggcactccag tctgggggac agagtgagac 180
cccatctcaa aaaagtgttt aattnantat acttgtgagt ggtctatttg catttnaaaa 240
ctgctttcta gaattaggat agctccctta ggtttaatgt tttggtgagc aggaatatca 300
gttacccctc cagatcttaa ttctagtttt tttatcactt tttcatgagg tgatctcatc 360
ctcatctcct agcatgtctg gcaattttga tttctgaact ctgtgctacc tcagaggcca 420
gcttccttag ggaaaaatca gtgctgaaat aaagttatat ttccttttct gctctaaata 480
tatagtgggg gaataagaga aatgaagagg aattcctgag aacgtaatta ctagaaactc 540
ccctctccca cgtaatgtct ctcacacacc atggacccct attcccccaa tttgcgaccc 600
cccaccccac cccacaacag gtggtgatct ttgtgaagtc tgtgcagcgg tgcattgcct 660
tggcccagct actagtggag cagaacttcc cagccattgc catccaccgt gggatgcccc 720
aggaggagag gntttaaaga ttttcaacga cgaattcttg tggctaccaa cctatttggc 780
cgaggcatgg acatcgagcg ggtgaacatt gcttttaatt atgacatgcc tgaggattct 840
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acatttgtgt ccgatgagaa tgatgccaag atcctcaatg atgtgcagga tcgctttgag 960
gtcaatatta gtgagctgcc tgatgagata gacatctcct cctacattga acagacacgg 1020
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ggggtgaagg agacactact gcccccaccc ctgacagccc ccaccccatg gcttccatct 1140
tttgcatcac caccactcct gaacccccat ttctgatttg tcagaatttt tttttaacaa 1200
aactaaaaat gaaacacatg tgtctgtggt atctaaaaaa aaaaaaaaaa aaawwggggg 1260
ggsgcccgta cccattggnc ct 1282

<210> 159
<211> 1505
<212> DNA

<213> Homo sapiens

<400> 159
ttacatgttg cagaagctaa ttgaagagac agataggttt gtagtgttca cagaagagga 60
atcaggcatg agtgaccagt tgtgtggcat tgctgcctgc cagacggatg acatatacaa 120
ccgaaactgc cttattgaat tggtcaacct gtcagatggt tcttcgtgga gcagagacak 180
aaggctgtgt cattgtgtca gctgccaaag cccaactgct gcagtgccag caccatccag 240
cctggtatgg tgatacattg aagcaaaaga catcctggac ttgcctcttg gatggcatgc 300
agtactttgc caccactgaa agcagcccca cagagcagga tggccgacag ctctggttag 360
aggtgaagaa tatcgaggag caccggcagc gtagtctgga ctctgtgcag gagctgatgg 420
agagtgggca ggcagtgggc ggcatggtta ccacaaccac agattggaac cagccagctg 480
aggcacagca agcccagcaa gtccagcgga tcatttcgcg ttgcaactgc cgaatgtact 540
atattagtta cagccatgac attgatcctg aactagcaac tcagattaag ccacctgaag 600
ttcttgagaa ccaggaaaag gaagatctcc taaagaagca ggaaggggct gtggatacct 660
tcacccttat ccaccatgag ctggaaattt ccaccaaccc agctcagtat gccatgatcc 720
tggacattgt caacaacctg ctgctccatg tagaacctaa gcggaaggaa catagtgaga 780
agaagcaacg ggtcaggttc cagcttgaga tctctagcaa tccagaggag caacgcagca 840
gcatactgca tttgcaggag gctgtgcggc agcatgtggc ccaaatacga cagctggaga 900
agcagatgta ttctatcatg aagtctttgc aggatgacag caagaatgag aatctgcttg 960
acctgaacca gaagcttcag ttgcagctaa accaggagaa ggccaacctg cagctggaaa 1020
gtgaagaact gaatatcctc atcaggtgtt ttaaggattt ccaactgcag cgggctaaca 1080
agatggagct gcgaaagcac aagaagatgt gagtgtggtc cgtcgcactg agttttactt 1140
tgctcaggca cggtggcgcc tgacagagga agatggacag ctgggaattg ctgaattaga 1200
actgcagagg ttcctctaca gcaaggtgaa taagtctgat gacacagcag aacatcttct 1260
ggagttgggc tggtttacca tgaacaacct cctccccaat gctgtctata aggtagtact 1320
gcggccccag agctcctgcc agtctgggcg acagctagct ctccgcctct tcagcaaagt 1380
tcggcccccct gttgggggta tctctgttaa ggagcatttt gaggtaaatg tggtgctctc 1440
accatccagc tgacacacca ttcttccaca gatgatgggc ttttctttcc tggccgaagt 1500
gtgga 1505

<210> 160
<211> 736
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (718)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (723)
<223> n equals a,t,g, or c

<400> 160
aggcacgagg gacacttggg gtctggacgc aacggcggcg ggagcatgaa cgcccctcca 60
gccttcgagt cgttcttgct cttcgagggc gagaagatca ccattaacaa ggacaccaag 120
gtacccaatg cctgtttatt caccatcaac aaagaagacc acacactggg aaacatcatt 180
aaatcacgtg cctgcttccc cttcgccttc tgccgtgatt gtcagtttcc tgaggcctcc 240
ccagccacgc ttcctgtaca gcctgcagaa ctgtgagtca attaaacctc ttttcttcat 300

aaattaccca gtttctcata gttctttata gcagtgtgaa aacagactaa tggacccttc 360
tggttgaagg aatgcagcca ttctgcttgt ttgactatgt cctttctatt catctctatt 420
tcctgggagg tgtttatcca agtgcaatag gaggtattgg tgaccgcaca gtcccctcag 480
tgttctgcta gtaaatagtt gaaggttgat cattgatctt ctgcgttttc agtctggcat 540
ggaaaagccc ctgtgcaact ggtaaagata tcaataagca cctggtgggt ggcgggggta 600
gtccaggctt gtcttgcaac tgtatgttct cttcagaccc ctccctggcg atgccagatt 660
cactgggctg gcagattctg ccccccccaa aaaaaaaaaa aaaatattaa taataaanaa 720
aanagactcc caggga 736

<210> 161
<211> 995
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (59)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (889)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (899)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (928)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (933)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (938)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (974)
<223> n equals a,t,g, or c

<400> 161
gggtcgaccc acgcgtccgg gcggcctcgg cagcggtgtt ctcgcgcttg cgaasgggnc 60

tccggctcgg ctcgcgggga ctgtgcacga ggttggcgac gcgccccgcc gggccccaga 120
tcaggccgca gagatcggga gccgcgggag cactaaggcg caagggccac agcagcagcc 180
gggctcagag ggtcccagct atgccaaaaa agttgcgctc tggcttgctg ggctgcttgg 240
agctggtggg actgtgagcg tcgtctatat ctttggaaac aacccggtgg acgaaaatgg 300
tgccaagatt cctgatgagt tcgacaatga tccaattctg gtacagcagt tgcgccggac 360
atacaaatat ttcaaagatt atagacagat gatcatcgag cccaccagcc cttgccttct 420
cccagaccct ctgcaggaac cgtactacca gccaccctac acgctcgttt tggagctcac 480
cggcgtcctc ttgcatcctg agtggtcgct ggccactggc tggaggttta agaagcgccc 540
aggcatcgag accttgttcc agcagcttgc ccctttatat gaaattgtca tctttacgtc 600
agagactggc atgactgcgt ttccactcat tgatagtgtg gaccccccatg gcttcatctc 660
ctaccgccta ttccgggacg ccacaagata catggatgga caccatgtaa aggatatttc 720
atgtctgaat cgggacccag ctcgagtagt agttgtggac tgcaagaagg aagccttccg 780
cctgcagccc tataacggcg ttgccctgcg gccctgggac ggcaactctg atgaccgggt 840
cttgttggat ctgtctgcct tcctcaagac cattgcactg aatggtgtng gaggacgtng 900
cgaaccgtgc tgggagcatt atgccctngg ganggatnga ccccgctggg cggcttttyc 960
aaacagcggc aaancgggct tagaagcagg gagga 995

<210> 162
<211> 1125
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (972)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1023)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1077)
<223> n equals a,t,g, or c

<400> 162
gccctagtac ggtccggaat tcccgggtcg acccacgcgt ccgcccacgc gtccgcgctg 60
gtgttgcggc gctggcgaca gtcggggttg cgagcggccc ggggccgggg cggccagggc 120
cgctgcagga cgagaccctg ggtgtggcgt ccgtgccctc gcagtggagg gccgtccagg 180
gcatccgcgg ggagacgaaa agttgccaga cggccagcat tgccactgcc agtgcatccg 240
cccaggccag gaatcatgtg gacgcccagg tgcagacgga ggcccccgtg cctgtcagcg 300
tgcagccccc gtcccagtay gacataccca ggctcgcagc ctttcttcgg agagtggagg 360
ccatggtcat ccgagagctg aacaagaatt ggcagagcca cgcgtttgat ggcttcgagg 420
tgaactggac cgagcagcag cagatggtgt cttgtctgta taccctgggc tacccgccag 480
cccaagcgca gggtctgcat gtgaccagca tctcctggaa ctccactggc tctgtggtgg 540
cctgtgccta cggccggctg gaccatgggg actggagcac gcttaagtcc ttcgtgtgtg 600
cctggaacct ggaccggcga gacctgcgtc cccagcaacc gtcggccgtg gtggaggtcc 660
ccagcgctgt cctgtgtctg gccttccacc ccacgcagcc ctcccamgtc gcaggagggc 720
tgtacagtgg tgaggtgttg gtgtgggacc tgagccgtct tgaggacccg ctgctgtggc 780

gcacaggcct gacggatgac acccacacag accctgtgtc ccaggtggtg tggctgcccg 840
agcctgggca cagccamcgg ttycaggtgc tkagtgtggc cacygacggg aaggtgctac 900
tctggcargg catcggggta rgccagctgc agttcacaga rggcttcgcc tggttcatkc 960
agcagctgcc anggagcacc aagctcaaga agcatccccg cgggagaccg aggtgggcgc 1020
canggcaggc tttcttccag tttgacctca ggttttcatt ttggcaggaa gcggttnccg 1080
ttcaattttc ctggcattgg agagcagcct taaggggtgc ccatt 1125

<210> 163
<211> 423
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (390)
<223> n equals a,t,g, or c

<400> 163
gggtcgaccc acgcgtccga gatggcgttt cgcagcaaga ggccggagca cggcgggccc 60
ccggagctgt tttatgacaa gaatgaagcc cggaaatacg tgcgcaactc acggatgatt 120
gatgtccaga ccaaaatggc tgggcgagct ttggagctcc tttgtctgcc ggaggtcagc 180
cctgttacct cttggatatt ggctgtggtt ctgggctgag tggagattat ctctcggatg 240
aagggcacta ctgggtaggc atcgacatca gccctgccat gctggatgcg gccttggacc 300
gagacactga gggagacctg cttctggggg acatgggcca gggcatcccc ttcaaaccag 360
kttcattgat ggatgtatca gcattctgcn aatcagtggc tctgtaatgc aaaccaagaa 420
gtc 423

<210> 164
<211> 1642
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1614)
<223> n equals a,t,g, or c

<400> 164
acccacgcgt ccggcggctg gcggagcaga acggattgca gggtcagcca tgtcatctga 60
gcctccccca ccaccacagc cccccaccca tcaagcttca gtcgggctgc tggacacccc 120
tcggagccgt gagcgctcac catcccctct gcgsggcaac gtggtcccaa gcccactgcc 180
cactcgccgg acgaggacct tctcggcgac ggtgcgggct tcacagggcc ccgtctacaa 240
aggagtctgc aaatgcttct gccggtccaa gggccatggc ttcattaccc cagctgatgg 300
cggccccgac atcttcctgc acatctctga tgtggaaggg gagtatgtcc cagtggaagg 360
cgacgaggtc acctataaaa tgtgctccat cccacccaag aatgagaagc tgcaggccgt 420
ggaggtcgtc atcactcacc tggcaccagg caccaagcat gagacctggt ctggacatgt 480
catcagctcc taggagatgg tggaagcacc ccttgtcctg tgcttgtggg agactttgcg 540
gggaggaggc agcagacact ggagatgaca ttcttccaca cgagacgggg cttcagccgg 600
gcatggtccc tctcaagtat ctcctggagg aaggggtatg gggggcaggt gtggggtgtg 660
gggtgttccc ggccatcagc acagcctatg accattgcaa caacctctca ccatctgaag 720
agcattaaaa gcatttaaaa aggaraggtg cccactggtg gctgagtgga ggttccaacc 780

ccatcccagg gagtggatca agggtggtat ttctccagct gctcagacac atgggctcaa 840
cccacagaat ccctcttcct cctggagctg gaggccccag attcccagat ctggccccct 900
ggcagcctga cagggacctt gcgtgacttc tccaaggcaa atttccacct aagtgcccct 960
tgcgcctctc ctggggcctg ggcaaagcag ttttctaatt cttggcttgg ttggttctag 1020
gggagctggc ttgaagtggg kggggaaagg cgggggtggc ggtctttgga ttggacggat 1080
gttgcctttt ggtgcctttg cagtgggagg cggcatagct gcctgtctgg ggaagacagt 1140
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gcatcctgac agcctggcaa agtcaagaaa gttgaaggag aaacatacct ttggagaggg 1440
ggttttcttt aaaactagtg ttaagaaatg cttagggatt ttttttttct tatttttcat 1500
aactaaagct ttcacccaga gccggctctg tttgcacttt gctgccgaca ttgcaaactt 1560
tttggcaggg tgggagactg agtctcattc tgtcamccag gctggagtgc agtngcccga 1620
tctcagcttt actgcaacct ct 1642

<210> 165
<211> 1115
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (390)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (394)
<223> n equals a,t,g, or c

<400> 165
aggaatgccg agtactgcag ggctccccca gggagtatgt gaatgccagg cactgtttgc 60
cgtgccaccc tgagtgtcag ccccagaatg gctcagtgac ctgttttgga ccggaggctg 120
accagtgtgt ggcctgtgcc catcaagtgg atggcgctgg agtccattct ccgccggcgg 180
ttcacccacc agagtgatgt gtggagttat ggtgtgactg tktgggagct gatgactttt 240
ggggccaaac cttacgatgg gatcccagcc cgggaggatc cctgacctgc tggaaaaggg 300
ggagcggctg ccccagcccc ccatctgcac cattgatgtc tacatgatca tggtcaaatg 360
ttggatgatt gactctgaat gtcggccaan attncgggag ttggtgtktg aattctcccg 420
catggccagg gacccccagc gctttgtggt catccagaat gaggacttgg gcccagccag 480
tcccttggac agcaccttct accgctcact gctggaggac gatgacatgg gggacctggt 540
ggatgctgag gagtatctgg taccccagca gggcttcttc tgtccagacc ctgccccggg 600
cgctgggggc atggtccacc acaggcaccg cagctcatct accaggagtg gcggtgggga 660
cctgacacta gggctggagc cykctgaaag aggaggcccc caggtctcca ctggcaccct 720
ccgaagggct ggctccgatg tatttratgg tgacctggga atgggggcag ccaaggggct 780
gcaaagcctc cccacacatg accccagccc tctacagcgg tacagtgagg accccacagt 840
acccctgccc tctragactg atggctacgt tgcccccctg acctgcagcc cccagcctga 900
atatgtgaac cagccagatg ttcggcccca gccccccttcg ccccgagagg gccctctgcc 960
tgctgcccga cctgctggtg ccactctgga aaggsccaag actctctccc cagggaagaa 1020
tggggtcgtc aaagagtttt tgcctttggg ggtgccgtgg agaaccccga gtattgacac 1080
cccaggggag ggagcttgcc cttcagcccc acctt 1115

<210> 166
<211> 1066
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (10)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (739)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (968)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1023)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1025)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1042)
<223> n equals a,t,g, or c

<400> 166
gggcacgagn cacctgagcc ccttgtctcg caccggctcc caggagggca cctccatgga 60
gggctcccgc cccgctgccc ctgccagagc caggcaccct caagaccagt ctggtggcta 120
ctccaggcat tgacaagctg accgagaagt cccaggtgtc agaggatggc accttgcggt 180
ccctggaacc tgagccccag cagagcttgg aggatggcag cccggctaag ggggagccca 240
gccaggcatg gagggagcag cggcgaccgt ccacctcatc agccagtggg cagtggagcc 300
caacgccaga gtgggtcctc tcctggaagt cgaagctgcc gctgcagacc atcatgaggc 360
tgctgcaggt gctggttccg cagtggagaa gatctgcatc gacaagggcc tgacggatga 420
gtctgagatc ctgcggttcc tgcagcatgg caccctggtg gggctgctgc ccgtgcccca 480
ccccatcctc atccgcaagt accaggccaa ctcgggcact gccatgtggt tccgcaccta 540
catgtggggc gtcatctatc tgaggaatgt ggacccccct gtctggtacg acaccgacgt 600
gaagctgttt gagatacagc gggtgtgagg atgaagccga cgaggggctc agtctagggg 660
aaggcagggc cttggtccct gaggcttccc ccatccacca ttctgagctt taaattacca 720
cgatcagggc ctggaacang cagagtggcc ctgagtgtca tgccctagag acccctgtgg 780
ccaggacaat gtgaactggc tcagatcccc ctcaacccct aggctggact cacaggagcc 840

ccatctctgg ggctatgccc caccagagac cactgccccc aacactcgga ctccctcttt 900
aagacctggg ytcagtgctg gcccctcagt gcccaccact cctgtgctac ccagcccccca 960
gaggcagnaa rccaatgggt cactgttgcc cctaaagggg ggtttttgaa ccaaggggga 1020
aancnacggg gcctggttcc cntttggaaa ggtttcccct gggaaa 1066

<210> 167
<211> 657
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (278)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (564)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (597)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (602)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (635)
<223> n equals a,t,g, or c

<400> 167
gtcgcgagcg ctgccgtcgg gaggcgctcc gaggttcgag gctgtgcccc gcgaccccgc 60
cttcggcgct cggctcgcag gatggatccc gtacccggga cagactcggc gccgctggct 120
ggcctggcct ggtcgtcggc ctctgcaccc ccgccgcggg gkttcagcgc gatctcctgc 180
accgtcgagg gggcaccgcc agctttggca agagcttcgc gcagaaatct ggctacttcc 240
tgtgccttag ttctctgggc agcctagaga acccgcanga gaacgtggtg gccgatatcc 300
agatcgtggt ggacaagagc cccctgccgc tgggcttctc cccgtctgc gamcccatgg 360
attccaaggc ctctgtgtcc aagaagaaac gcatgtgtgt gaarctgttg cccctkggar 420
ccamggacac ggctgtgttt gatgtccggc tgagtgggaa gaccaagaca gtgcctggat 480
accttcgaat aggggacatg ggcggctttg ccatctggtg caagaaaggc caaggccccg 540
aggccagttg cccaaagccc cgangtcctc agcccgggac atgcaagggc ttctctntgg 600
angcagccag ccagcccaag ttaagggcgg gcctncttgg aagccggaca agcgttc 657

<210> 168
<211> 1026
<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (1011)
<223> n equals a,t,g, or c

<400> 168
ggcacgagga gagatggagg ggcggcaggt gctggaggtc aagatgcagg tggagtacat 60
gtcattcagc gcacacgcgg acgccaaggg catcatgcag ctggtgggcc aggcagagcc 120
gkagagcgtg ctgctggtgc atggcgaggc caagaagatg gagttcctga agcagaagat 180
cgagcaggag ctccgggtca actgctacat gccggccaat ggcgagacgg tgacgctgcc 240
cacaagcccc agcatccccg taggcatctc gctggggctg ctgaagcggg agatggcgca 300
ggggctgctc cctgaggcca agaagcctcg gctcctgcac ggcaccctga tcatgaagga 360
cagcaacttc cggctggtgt cctcagagca agccctcaaa gagctgggtc tggctgagca 420
ccagctgcgc ttcacctgcc gcgtgcacct gcatgacaca cgcaaggagc aggagacggc 480
attgcgcgtc tacagccacc tcaagagcgt cctgaaggac cactgtgtgc agcacctccc 540
rgacggctct gtgactgtgg agtccgtcct cctccaggcc gccgcccctt ctgaggaccc 600
aggcaccaag gtgctgctgg tctcctggac ctaccaggac gaggagctgg ggagcttcct 660
cacatctctg ctgaagaagg gcctccccca ggcccccagc tgaggccggc aactcaccca 720
gccgccacct ctgccctctc ccagctggac agaccctggg cctgcacttc aggactgtgg 780
gtgccctggg tgaacagacc ctgcaggtcc catccctggg gacagaggcc ttgtgtcacc 840
tgcctgccca ggcagctgtt tgcagctgaa gaaacaaact ggtctccagg ctgtcttgcc 900
tttattcctg gttagggcag gtggtcctag acagcagttt ccagtaaaag ctgaacaaaa 960
aaaaaaaaaa aaaaaattgg gggggggccc gttacccatt tggcctttag ngggggtttt 1020
aaatta 1026

<210> 169
<211> 774
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (730)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (733)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (754)
<223> n equals a,t,g, or c

<400> 169
ggcataaaca tcgggtggtg ttcagatcct gctgccggca gctcgaggct aggatggctg 60
gagatgtgag ggcctttgtc tcatcacatc cgagcacagc tcagcaagat gctcttagct 120
agraaacaga ttttatgtgt taatgttaaa aattttgcag ttatttatct tgtggatatt 180

acagaagtgc ctgacttcaa caaaatgtat gagttatacg atccatgtac tgtcatgttt 240
ttcttcagga acaagcacat catgattgac ttggggactg gcaacaacaa caagattaac 300
tgggccatgg aggacaagca ggagatggtg gacatcatcg agacggtgta ccgcggggcc 360
cgcaaargcc gcggcctggt ggtgtccccc aaggactact ccaccaagta ccgctactga 420
ggcgccctca gtctgcgcgg ataaatgtcg tggagccctt tttgtatgga aacgttttaa 480
gctatttaaa gcctttggaa aatacaggaa gctccagggc tggagcacct ctgagatgga 540
attgataaca tggtcttaac tcaccgaaat aaacaagcac gtggtgagag gagcaggcct 600
acttgtttgt tctcaggaaa cttaatgaat agattactga ttttcctagt caaagttaat 660
tcttaccctt ggagtaaaac gaaggtgttt atcctgtgag cctgtgcgtt ttgcatactg 720
ggttggtttn ctngggcttc ggtgacagca tatnccgcga gctgggcttt aaca 774

<210> 170
<211> 402
<212> DNA
<213> Homo sapiens

<400> 170
ggcacgagcg gcggtggggc ggacagccgg ggtgcgcact tgggcccccc tggccatggc 60
ggcgaaggtg gacctgagca cctccaccga ctggaaggag gcgaaatcct ttctgaaggg 120
cctgagtgac aagcagcggg aggaacatta cttctgcaag gactttgtca ggctgaagaa 180
gatcccgaca tggaaggaga tggcgaaagg ggtggctgtg aaggtggagg agcccaggta 240
taaaaaggac aagcagctca atgagaaaat ctccctgctc cgcagcgaca tcaccaagct 300
ggaggtggac gccatcgtca acgccgccaa cagctccccg cccccgagga gcctaattaa 360
agatcttcgt tgtggcaaaa aaaaaaaaaa aaaaaaaaaa aa 402

<210> 171
<211> 796
<212> DNA
<213> Homo sapiens

<400> 171
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aagaagggct tctccatcgc caaggagggc gtggtgggtg cggtggaaaa gaccaagcag 180
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gcggagaaca tcgcggtcac ctccggggtg gtgcgcaagg aggacttgag gccatctgcc 420
ccccaacagg agggtgaggc atccaaagag aaagaggaag tggcagagga ggcccagagt 480
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actgccctcc ctcggcccca cccaccctct ggtccttctg accccactta tgctgctgtg 720
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aaaaaaaagg gggccc 796

<210> 172
<211> 478
<212> DNA
<213> Homo sapiens

<400> 172
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ccacccaccc tctggtcctt ctgaccccac ttatgctgct gtgaattttt tttttaaatg 420
attccaaata aaacttgagc ccactcctaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 478

<210> 173
<211> 656
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (59)
<223> n equals a,t,g, or c

<400> 173
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ctgcccttgg gatgggggcgc tcctgaatgt acgtgggccc cggtgtttac aaggaggtga 120
tcatctacaa cctctgccag aagcaggtgg tggagaagat accactgccc tttttgcca 180
tgtccctgag cctgtccccc gggacccacc tcctggctgt tggctttgct gagtgcatgc 240
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tgcacctgtg caggtttaca cckccgcca ggctgctctt cacggccgcc cgcaacgaga 360
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cctcatgctg ggacaggcca ggattcacgt aaatcgcctg gagcaagctg ttgtaaattt 540
ggcgccctgt gaatactttc atacctgttg ccctttgcc taagaaatct ttaatgtttc 600
tatcttgtaa taaacatggg catttattgc aaaaaaaaaa aaaaaaaaaa aaaaaa 656

<210> 174
<211> 1891
<212> DNA
<213> Homo sapiens

<400> 174
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tccaaacctc cgaccagcgc tacgtccttt acccgaacaa ctttcaattc cagtacgatg 180
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<210> 175
<211> 2161
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2153)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2160)
<223> n equals a,t,g, or c

<400> 175
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aatgaatgta ttgaaaaagt tgaaattgct ggtcctggtt ttattaatgt ccacttaaga 540
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a 2161

<210> 176
<211> 2411
<212> DNA
<213> Homo sapiens

<400> 176
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ctcatcmaaa tgctgctgta tttatgagaa acctcgggcc tttggcgaga gctccacgga 240
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<210> 177
<211> 1338
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1234)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1276)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1289)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1326)
<223> n equals a,t,g, or c

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caacanattt gaagcccg 1338

<210> 178
<211> 1614
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1213)
<223> n equals a,t,g, or c

<400> 178
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cctctaaagc tgagagcttg attccagggc ctgccctgct cctggtggca cccagtggcc 120
tgtactactg gtacctggtc accgagggcc agatcttcat cctcttcatc ttcaccttct 180
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gctagtctgt tcttcccgga catcttctgg tagccgtgca ggagagggct gggtggggca 780
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<210> 179
<211> 4292
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (654)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (4288)
<223> n equals a,t,g, or c

<400> 179

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acaagctgct atccaagcta tgaatggctt tcagatcggc atgaaacgct tgaaggtgca 240
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<213> Homo sapiens

<220>
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ccagagggaa gtgtggtgtg tgggcacaac gggaaacgct aaccaggcac agagctcaac 180
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tat 243

<210> 181
<211> 813
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (266)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (723)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (726)
<223> n equals a,t,g, or c

<220>
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<400> 181
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<210> 182
<211> 822
<212> DNA
<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (49)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (370)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (567)
<223> n equals a,t,g, or c

<400> 182
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<210> 183
<211> 1095
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1082)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1094)
<223> n equals a,t,g, or c

<400> 183
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<210> 184
<211> 3675
<212> DNA
<213> Homo sapiens

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<222> (2204)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3329)
<223> n equals a,t,g, or c

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<211> 1040
<212> DNA
<213> Homo sapiens

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<210> 186
<211> 817
<212> DNA
<213> Homo sapiens

<220>
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<222> (2)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (26)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (31)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (76)
<223> n equals a,t,g, or c

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<211> 1080
<212> DNA
<213> Homo sapiens

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ctggcccctc tcaggtcaga agacatgcct ggagggatgt ctggctgcaa agactatttt 1020
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<210> 188
<211> 1286
<212> DNA
<213> Homo sapiens

<220>

<221> misc feature
<222> (1245)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1254)
<223> n equals a,t,g, or c

<400> 188
gcatgattct tgttttgtag agatgcaggc tcaaaaagta atgcatgttt cttcagcaga 60
actgaattat tcactgccat atgactctaa acaccaaata cgtaatgcct ctaatgtaaa 120
gcaccatgac tctagtgctc ttggtgtata ttcttacata cctttagtgg aaaatcctta 180
tttttcatca tggcctccaa gtggtaccag ttctaagatg tctcttgatt tacctgagaa 240
gcaagatgga actgtttttc cttcttctct gktgccaaca tcctctacat ccctcttctc 300
ttattacaat tcacatgatt ctttatcact gaattctcca accaatattt cctcactatt 360
gaaccaggag tcagctgtac tagcaactgc tccaaggata gatgatgaaa tccccctcc 420
acttcctgta cggacacctg aatcatttat tgtggttgag gaagctggag aattctcacc 480
aaatgttccc aaatccttat cctcagctgt gaaggtaaaa attggaacat cactggaatg 540
gggtggaaca tctgaaccaa agaaatttga tgactctgtg atacttagac caagcaagag 600
tgtaaaactc cgaagtccta aatcagaact acatcaagat cgttcttctc ccccacctcc 660
tctcccagaa agaactctag agtccttctt tcttgccgat gaagattgta tgcaggccca 720
atctatagaa acatattcta ctagctatcc tgacaccatg gaaaattcaa catcttcaaa 780
acagacactg aagactcctg gaaaaagttt cacaaggagt aagagtttga aaattttgcg 840
aaacatgaaa aagartatct gtaattcttg cccaccaaac aagcctgcag aatctgttca 900
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tctatatgca taatatcaaa tatgaagata tgctaatgtg ttaatagctt ttaaaagaaa 1140
agcaaaatgc caataagtgc cagttttgca ttttcatatc atttgcattg agttgaaaac 1200
tgcaaataaa agtttgtcac ttgagcttat gtacagaatg ctatntgggg aacnctttta 1260
ggatgggttt tatttttcca tttttg 1286

<210> 189
<211> 1738
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1480)
<223> n equals a,t,g, or c

<400> 189
gcggcgccct cggagccaaa ggcgcgcggc ggacacggcg gggccctcgc gcgcctggag 60
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gtcgtggccc ccatggtgga ccagagcgag ctggcctgga ggctgctgag ccggcgccac 180
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taccggaagg agaacctgta ctgcgaggtg tgccccgagg accggcccct catcgtgcag 300
ttctgtgcca atgacccgga ggtgtttgtt caggcggctc tcctggctca ggattactgt 360
gacgccattg acctgaactt gggctgccca cagatgatag ccaagagagg tcactatggc 420

gcctttctgc aggacgagtg ggacctgctc caaagaatga ttttgctggc ccacgagaaa 480
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agcagaaggg gcccctgtcg ggtgcagcgt cctgggagca tatcaaggct gtgcggaagg 660
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gcctccggga cacgggtgtg cagggcgtca tgagcgcaga gggcaacctg cacaaccccg 780
ccctgttcga gggccggagc cctgccgtgt gggagctggc cgaggagtat ctggacatcg 840
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gcgtgtgcaa aagtgaacaa taaatcattt caaagatgaa aaaamaaaaa aaaaaaaa 1738

<210> 190
<211> 1923
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1829)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1875)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1910)
<223> n equals a,t,g, or c

<400> 190
agcacatcaa atgcccccac tccaagtacg ggtgcacgtt catcgggaac caggacactt 60
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atgaccgctt ccacgagatg cacgtggctc tggcccagaa ggaccaggag atcgccttcc 180
tgcgctccat gctgggaaag ctctcggaga agatcgacca gctagagaag agcctggagc 240
tcaagtttga cgtcctggac gaaaaccaga gcaagctcag cgaggacctc atggagttcc 300
ggcgggacgc atccatgtta aatgacgagc tgtcccacat caacgcgcgg ctgaacatgg 360
gcatcctagg ctcctacgac cctcagcaga tcttcaagtg caaagggacc tttgtgggcc 420

accagggccc tgtgtggtgt ctctgcgtct actccatggg tgacctgctc ttcagtggct 480
cctctgacaa gaccatcaag gtgtgggaca catgtaccac ctacaagtgt cagaagacac 540
tggagggcca tgatggcatc gtgctggctc tctgcatcca ggggtgcaaa ctctacagcg 600
gctctgcaga ctgcaccatc attgtgtggg acatccagaa cctgcagaag gtgaacacca 660
tccgggccca tgacaacccg gtgtgcacgc tggtctcctc acacaacgtg ctcttcagcg 720
gctccctgaa ggccatcaag gtctgggaca tcgtgggcac tgagctgaag ttgaagaagg 780
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ccgtggctgc ctgctacatg ccctgcttnc acgtggctgc acgctgacac acccacattc 1860
accaaaccca cccgngccct gggacgcaac cacgccagga ggaggacacn ggccgccgag 1920
agc 1923

<210> 191
<211> 250
<212> DNA
<213> Homo sapiens

<400> 191
ccaagtgtgt tgatacatta agctatgaga catctaaaat aatgaaactt ggaacttagt 60
ggaacatgta catgttttca gcatacttaa acccaaaaat cattaatttt cagaacttaa 120
tcagtgcttt tacatttgtt ttttctttta tgctagttgg aaatggagga tgaarataca 180
attgrtgtgt tccaacagca gacgggrggt gtctactgaa aagggaacct gcttctttac 240
tccagaactc 250

<210> 192
<211> 1902
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (8)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (19)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (763)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1898)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1900)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1901)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1902)
<223> n equals a,t,g, or c

<400> 192
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ccaaaaatca aaggaggtgc ggatgtttca gggggtgtca gtgccccara catcagcctt 120
ggtgaagggc atttragtgt taaaggttcc gggggtgagt ggaagggacc ccaagtctcc 180
tctgctctca acttggacac atctaagttt gctgggggcc ttcatttctc aggaccaaag 240
gtggaaggag gtgtgaaagg aggtcagatt ggactccagg ctcctgggct gagtgtgtct 300
gggcctcaag gtcacttgga aagtggatct ggaaaagtaa cattccctaa aatgaagatc 360
cccaaattta ccttctctgg ccgtgagctg gttggcagag aaatgggggt ggatgttcac 420
ttccctaaag cagaggccag catccaagct ggtgctggag acggcgagtg ggaagagtct 480
gaagtcaaac tgaaaaagtc caagatcaaa atgcccaagt ttaattttttc caaacctaaa 540
gggaaaggtg gtgtcactgg ctcaccagaa gcatcaattt ctgggtccaa aggtgacctg 600
aaaagttcaa aggccagcct gggctctctg gaaggagagg cagaggccga agcctcttca 660
ccgaaaggca aattctcctt atttaaaagt aagaagccac ggcaccgctg caaattcatt 720
cagtgatgaa agagagttct ctggaccttc cacccccgacg ggnacgctgg agtttgaagg 780
tggggaagtg tctctggaag gtgggaaagt taaagggaaa cacgggaagc tgaaattcgg 840
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tgagacaggc aagttacagg ggagtggggt gtccctggcc tctaagaagt cccgactgtc 960
ctcctcttct agcaatgaca gtgggaataa ggttggcatc cagcttcccg aggtggagct 1020

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ccgccatgtt cctgatatta gttctgattt ctttttaaca aatgttatca tgattaagaa 1800
aatttccagc actttaatgg ccaattaact gagaatgtaa gaaaattgaw gctgtacaag 1860
gcaaataaag ckgttattaa cctgaaaaaa aaaaaaanan nn                   1902
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<210> 193
<211> 560
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (20)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (528)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (535)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (559)
<223> n equals a,t,g, or c

<400> 193

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ttttgcttaa agctatttan gtgacactat agaaggtacg cctgcaggta ccggtccgga 60
attcccgggt cgacccacgc gtccggggtt gcagacggag gtcaggtctt cctctttcct 120
gagactggat ctgttcaaac agcaaacgcc cacagatggc ccagaggtgg tggtagtcag 180
ggtgtgtggg tgtttttagg gttctttagt gttgtttctt tcacccaggg gtggtggtcc 240
cagccagttt ggtgctgacg gtgagaggaa attagaatct gtttgcaaat tgtccaaccc 300
accccctcaa catgaggggc ttccattttc tgtgttttgt aagggaactg tttccttcat 360
gccgccatgt tcctgatatt agttctgatt tctttttaac aaatgttatc atgattaaga 420
aaatttccag cactttaatg gccaattaac tgagaatgta agaaaattga tgctgtacaa 480
ggcaaataaa gctgtttatt aaccttgaaa aaaaaaaaaa aaaggggngg cccgncccat 540
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tgccctaggg ggggttaant 560

<210> 194
<211> 590
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (589)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (590)
<223> n equals a,t,g, or c

<400> 194
ctgcaggtac cggtccggaa ttccgggtcg cccacgcgtc aggcggcggc gatgaccttc 60
tgccggctgc tgaaccggtg tggcgaggcg gcgcggagcc tgcccctggg cgccaggtgt 120
ttcggggtgc gggtctcgcc gaccggggag aaggtcacgc acactggcca ggtttatgat 180
gataaagact acaggagaat tcggtttgta ggtcgtcaga aagaggtgaa tgaaaacttt 240
gccattgatt tgatagcaga gcagcccgtg agcgaggtgg agactcgggt gatagcgtgc 300
gatggcggcg ggggagctct tggccaccca aaagtgtata taaacttgga caaagaaaca 360
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tggcacgccg ggggtcccgc agcatcctgt gagcatttcc gcggggaagc tgagcacgtg 480
aagctcgctg gttctgtgcg aagggtattc ctggtgctga ataaagggtg ttgctgtcaa 540
gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaann 590

<210> 195
<211> 691
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (10)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (579)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (618)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (639)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (657)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (672)
<223> n equals a,t,g, or c

<400> 195
attggcatcn tctgaaagcg ttttagacag gcagaatctc tggtctcccc tctctgcatt 60
ccccacccag tgaatgaatg agaatctgca tttcttgaga tcataagaat actgacatac 120
agatgagata aaactcatgt gaatatcagt tttaaggctg gtggttcatt tgttttggtc 180
atattgagtc aggattgact aatgaactgt agaggttttg cattatgcaa atgctcttaa 240
tttcttgtat taggaattag acgctccccc ccaagtctta aataatgttt taatctgtat 300
cctttttatta taagaagatt agtaatattc tacagataat aacaacaact ggtatagtat 360
attttattta cattcttcat tcttaggaga aaatgctgag aagcttctgc agttcaagcg 420
ttggttctgg tcaatagtag agaagatgag catgacagaa cgacaagatc ttgkttactt 480
ttggacwtca agcccatcac tgccagccag tgaagaagga ttccagccta tgccctcaat 540
cacaatawga ccaccagatg accmacatct tcctactgna aaatacttgc atttcttgga 600
ctttaccttc ccactctntt cctttaaaca ggattcttna aaccggaaat tggttanctc 660
gccatttagg anccaaaaat tttgggtttt g 691

<210> 196
<211> 1772
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1749)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1769)
<223> n equals a,t,g, or c

<400> 196
gnataatgct ggccattttg cctttctgac atttccttgg gaatctgcaa gaacctcccc 60
tttcccttcc cmcaataaga ccatttaagt gtgtgytaaa caactacrga atactaaata 120
aaaagtttgg ccaaaaccaa ccatgaagct gcaaaggtgc ttgctcttac tstttcaaat 180

ttttgcaact ctartgtctc actttttaaag gaacagcttg attgcaaagg agaaaataga 240
taagcaatga akttatctcc aacttcctaa aggcttatga cttctaaaaa gtgaatctat 300
cagcattcca catcagattt aaagcatcaa atgcctgtga aacagcaaag atggttgaag 360
attgtgctca ttatgtttgt ggagtgctga ttgattcaca gtagataacg ctggcagtaa 420
gagaaatcaa atgctaagag ttgttgaagc agaaggcggc tgattgttgg taagtcagtg 480
cagttgcata agcagtgctg tcagaattgg tttggtgcag gcaatagatt ttgccttcaa 540
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stggtagtta cttaagtaat tgaccaaatg gaaaagggga agtaattaag gaaattggta 660
agtggaggta gtcaggargt tctygtggty cttyacayag attttacagc tttggstttc 720
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cttgaagata gtataggata tagagattgt accaaatagg aatataagga gtatgttaaa 1440
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740
aaaaaagana aaaaaaaaag ggggggccnc cc 1772

<210> 197
<211> 675
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (657)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (671)
<223> n equals a,t,g, or c

<400> 197
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gtgggaactg ggtactatgt agagaagaca gctgaggatg ccaaggactt cttcaagagg 360
aagatagatt ttctaaccaa gcagatggag aaaatccaac cagctcttca ggagaagcac 420

gccatgaaac aggccgtcat ggaaatgatg agtcagaaga ttcagcagct cacagccctg 480
ggggcagctc aggctactgc taaggcctga gagtttttgc agaaatgggg cagagggaca 540
ccctttgggc gtggcttcct ggtgatggga agggtcttgt gttttaatgc caataaatgt 600
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<210> 198
<211> 557
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (451)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (461)
<223> n equals a,t,g, or c

<220>
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<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

<220>
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<222> (492)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (495)
<223> n equals a,t,g, or c

<400> 198
tttaggtgac acgtatagaa ggtcgcctgc aggtaccggw ccggaattcc gggtcgaccc 60
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<210> 199
<211> 2611
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (3)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2549)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2560)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2585)
<223> n equals a,t,g, or c

<400> 199
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cgctgtgagg acatcctgca gcagctgcag gccgtggtac cccagataga catggaaggg 240
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tgggnccccg gaaagagatg ttacttggac c 2611

<210> 200
<211> 2316
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2280)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2282)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2302)
<223> n equals a,t,g, or c

<400> 200
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ccctcagctc tcccctgccc ttcactcatg gaagtcttca ggcaagtttt tcacttacaa 180
gggactgcgt atcttctacc aagactctgt gggtgtggtt ggaagtccag agatagttgt 240
gcttttacac ggttttccaa catccagcta cgactggtac aagatttggg aaggtctgac 300
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gagaccacat cactattcca tatttgagca ggccagcatc gtggaagcgc ttttgcggca 420
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<210> 201
<211> 1147
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (5)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (12)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (19)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1145)
<223> n equals a,t,g, or c

<400> 201
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cttcgttcga gaacaactgt gagatcggct gctttgccaa gctcaccaac acctactgtc 180
tggtagcgat cggaggctca gagaacttct acagtgtgtt cgagggcgag ctctccgata 240
ccatccccgt ggtgcacgcg tctatcgccg gctgccgcat catcgggcgc atgtgtgtgg 300
ggaacaggca cggtctcctg gtacccaaca ataccaccga ccaggagctg caacacattc 360
gcaacagcct cccagacaca gtgcagatta ggcgggtgga ggagcggctc tcagccttgg 420
gcaatgtcac cacctgcaat gactacgtgg ccttggtcca cccagacttg gacagggaga 480
cagaagaaat tctggcagat gtgctcaagg tggaagtctt cagacagaca gtggccgacc 540
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cttcaattga agaccaggat gagctgtcct ctcttcttca agtcccccctt gtggcgggga 660
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tgcaaaaacc tgctctgttg tgctggctgg caggccctgt ggctgctggc tgagggttct 1080
gctgtcctgt gccaccccat taaagtgcag ttccctccgg aaaaaaaaaa aaaaaaaggg 1140
cggcnac                                                           1147
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<210> 202
<211> 688
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (477)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (684)

<223> n equals a,t,g, or c

<400> 202
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ggagtcgggc cgcgactgtg gtcgttttta taccttcccg cgcggacgcc ggcgctgcca 120
acggaagggc gggtaggacg gagtttcgtc atgttggcca ggcccatttg agatctttga 180
agatatcctc aacgtgaggc tctgctgcca tgaaggtgaa gattaagtgc tggaacggcg 240
tggccacttg gctctgggtg gccaacgatg agaactgtgg catctgcagg atggcattta 300
acggatgctg ccctgactgc aaggtgcccg gcgacgactg cccgctggtg tggggccagt 360
gctcccactg cttccacatg cattgcatcc tcaagtggct gcacgcacag caggtgcagc 420
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cgcccctgag ctgcaacaag gtggaaacaa gggctggagc tgcgtttgtt ttgccatcac 600
tatgttgaca cttttatcca ataagtgaaa actcattaaa ctactcaaat cttaaaaaaa 660
aaawaaawaa atctcggggg gggncccg 688

<210> 203
<211> 304
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (269)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (287)
<223> n equals a,t,g, or c

<400> 203
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taactctaga gcccattctc ctaaccactg agccatgatt gtcttacaat tttgaatact 120
gcaaaactgg aagaattgtc tggctattat ctaagctgtt cataagctgg aacaagtaga 180
tctgagggta agaggagttc tgttttaact aggactgagt ttcaaataga gatgtttcag 240
actatagagg gggaaaaatg gcckgggang tccataaatc taagccngtt tcatggatgt 300
tttt 304

<210> 204
<211> 417
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (380)
<223> n equals a,t,g, or c

<400> 204
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tgatggccct gcaaggctgt gggctccgac ctcaccggga gtcgamarcg agaggttcgc 120
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cagtccgcgt ccacagactc tgacgaagac gtggatctgc tctcgcttta gctgctcgcg 240
gtcctccaga tcatgtccgc gactcctgcg actccgcgcg gaaaaaaaag tttgccaggc 300
gtggactcaa tgacytttcc aastgtgcgc ctcgytgcct ggaccggttt gagcgcggtt 360
gcccaagttg aactttttgn ggggagggtt ttctctaagg gctgttgtct caatggg 417

<210> 205
<211> 551
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (450)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (458)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (471)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (484)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (519)
<223> n equals a,t,g, or c

<400> 205
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tttttttttt tggtttccag agtttggctt tattttgcag tacagaaatc atctggagcc 120
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gcggggccac gcagggatgc tgttcccaan tcacgganta tctggtgggc ntcgcaatgg 480
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gaccgcggag g 551

<210> 206
<211> 1101

<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (21)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (479)
<223> n equals a,t,g, or c

<400> 206
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ggtccccgcg cgccccgggt cggaggcaga cccctgggtt tgggggacat gggcatttgg 120
ggcgcctgaa cccaagacct ctggatgagc tgccccgttc agaccatgga tcctgaggtg 180
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ggtgccaccg actggggtga cacgcaggcc tatctggcgg acccactggg ggtgggcgct 540
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cacgagtcta caggaatctt ctttgtggag acacagaacg tgcggagatt gcccgagacg 960
gagatgtggg ctgaactctg cccctcgcca aaggcgccat catcctctac aaccgggttc 1020
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aataaacgac tttattcttg g 1101

<210> 207
<211> 515
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (428)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (439)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (449)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (456)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (474)
<223> n equals a,t,g, or c

<400> 207
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acactgcgag aatacaaggt ggtggggcgc tgcctgccca cccccaaatg tcgcactccg 120
ccgctgtatc gcatgcgaat ctttgcacct aatcacgtgg tcgccaagtc ccgcttttgg 180
tactttgtgt ctcagctgaa aaagatgaag aagtcctcag gggaaatcgt ctactgtgga 240
caggtgtttg agaaatcccc cttgcgagtg aagaacttcg gcatctggct gcgctatgac 300
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ccgtcaccca gtggttaccg agacatgggc gcccgacacc gttgcccgag cgcattcgat 420
tccagatnct tgaagtggna ggagattgnc agccancaat tgccgccggg ccancattca 480
agcatttcca aggattccaa gatcaattcc cattg 515

<210> 208
<211> 269
<212> DNA
<213> Homo sapiens

<400> 208
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aatctggaca tcattttccc tttcagagca tagaatgcag ggggatccag ggaatgggtt 180
aacagaagag gaagctggwt caaggagacc tttgcgtacc aggtgaaggt gtttgaactt 240
tgttcttgca ggcaggcaga gcacggaca 269

<210> 209
<211> 734
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (278)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (732)
<223> n equals a,t,g, or c

<400> 209
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ccgcggacgc ccgctgagct tggcgcacgg gccgaccagg agctggtgac tgccctcatg 120
tgtgatttgc ggcggccagc ggcaggtggg atgatggact tggcctacgt ctgtgagtgg 180
gagaaatggt ccaagagcac ccactgccca tcggtgcccc tggcctgcgc ctggtcctgc 240
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aaactggccc tgcacgtgga gaagtcgggc gcctccagct tcggggagaa gttctcccga 600
gtcaagttct caccygttct cacgctgttc ggcggcaagc catggagggc tggatcgcgg 660
tgacggtcag cggcctggtc accgtgtccc tgctgwaasc agcgggcagg tgctgacgtc 720
caccgagagc tntt 734

<210> 210
<211> 658
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (561)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (567)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (577)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (580)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (636)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (654)
<223> n equals a,t,g, or c

<400> 210

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aaatggcatg tcatttttcg tgcagacggc tgggagcaac atattaccgc ccgctatctg 120
gtcggtgccg atggcgcaaa ctcgatggtg cggcgacatc tctacccgga tcatcaaatc 180
cgtaaatatg tcgctatcca gcagtggttc gcggagaaac atccggtgcc gttctactcc 240
tgcatctttg ataattcgat aactaactgt tattcatgga gtatcagcaa agacggktat 300
tttatctttg gcggtgccta tccaatggaa agacggtcag acgsgtttca sgacgcttra 360
agagaaaatg agcgcctttc agttccagtt tggtaagacg gtgaaaagcg aaaaatgcac 420
gggtgctgtt tccctcgcgc tggcaggatt ttgtctgcgg taaggacaac gcctttcttg 480
attggtgaac ggcgggattt atcagcgcca gctcgctgga agggattagc tatgcgctgg 540
atagcacaga catttctgcg ntcgtgntac tgaacanccn gagaagctca ataccgttac 600
tggcgcgcca cccgaaactg ggttaaactc ttcggnaaga tataaaaagc catnctga 658

<210> 211
<211> 204
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (91)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (94)
<223> n equals a,t,g, or c

<400> 211
attcggagag ccatctctga cagttagagc cgatatcact ggaagatatt caatcgtctc 60
tatgcttacg acctgcagat acagtctgtt nttncacatg aagaaagtct caagttgctg 120
aagactgaat tgtaagaaaa atctccagcc cttctgtctg cagcttgaga cttgaaccag 180
agagtgtgag agctgctgtt ggag 204

<210> 212
<211> 1271
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1222)
<223> n equals a,t,g, or c

<400> 212
ttccgcagcc ttgccccagc ccactccccc tctcacccta ccacagagca tggtaaatac 60
caagcccgag aagacggagg aggactcaga ggaggtgagg gagcagaaac acaagacctt 120
cgtggaaaaa tacgagaaac agatcaagca ctttggcatg cttcgccgct gggatgacag 180
ccaaaagtac ctgtcagaca acgtccacct ggtgtgcgag gagacagcca attacctggt 240
catttggtgc attgacctag aggtggagga gaaatgtgca ctcatggagc aggtggccca 300
ccagacaatc gtcatgcaat ttatcctgga gctggccaag agcctaaagg tggacccccg 360
ggcctgcttc cggcagttct tcactaagat taagacagcc gatcgccagt acatggaggg 420

cttcaacgac gagctggaag ccttcaagga gcgtgtgcgg ggccgtgcca agctgcgcat 480
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cctggacccc gtcgaggtct acgagtccct ccctgaggaa ctccagaagt gcttcgatgt 600
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gctggtctac caggtagttg gggagggtcc ccagccaagg ggccggctct cgtcactggg 1140
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aaaaaaaaaa g 1271

<210> 213
<211> 1025
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (991)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1007)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1019)
<223> n equals a,t,g, or c

<400> 213
cggacgcgtg ggcgagcgtg atagccaaca ggaaccggga gcggggtccc gggactggga 60
agaaacggcg gccgggaggg ggctccgggg accatggggc tcctgaccat tctgaagaag 120
atgaagcaga aagagcggga gctgcgactg ctcatgcttg gcctggacaa tgctggaaag 180
acaaccatcc tgaagaagtt caatggggag gacatcgaca ccatctcccc aacgctgggc 240
ttcaacatca agaccctgga gcaccgagga ttcaagctga acatctggga tgtgggtggc 300
cagaagtccc tgcggtccta ctggcggaac tactttgaga gcaccgatgg cctcatctgg 360
gtagtggaca gcgcagaccg ccagcgcatg caggactgcc agcgggagct ccagagcctg 420
ctggtggagg agcgcctggc cggagcaacc ctcctcatct ttgctaataa gcaggacctg 480
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caccactggt gcatccaggg ctgcagcgcc gtcaccgggg agaacctgct gccgggcatc 600
gactggctcc tggatgacat ttccagccgc attttcacag ctgactgaac cactccagat 660
gcccccacc tagcagtcca ggtccctcaa ccttcaccaa acactaccca tgggggttg 720
ggagtcagcc ggccaaacta acactccccc tcctccaccc cagcctgctg ctgctactgc 780
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ctctctggct cctgacctgg cctttggcta ccataccaag aagagagggc tgggcgggga 900
ggagctgcta ctgctgctac cgaggctgtg ggcctcatcc ttcactcagt tgtgaaataa 960
accgctcctt gccccgmaaa aaaaaaaaaa naaaaaaaaa aaaaaanccc gggggggnc 1020
ccgga 1025

<210> 214
<211> 351
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (332)
<223> n equals a,t,g, or c

<400> 214
ggcacgagtr aactatatac ctcaaagaat tagaaaaaga agaacaaact aagctcaaag 60
ttagcagaag gaaggaaata gtaaatatta cagcagaagt aaagtagagg ctagaaaaat 120
aataaaaaag atcaacaaaa tggtatttgt tctcatacta tgataaagac atacttgaga 180
accgcattat ttatggggaa aagaagttta attgactcac agttccacag gctgtacagg 240
aggcatggct tagggaggcc tcagggaaac ttagratcca tggtggaagg tgkargagga 300
agcatgcacc atcttcactg gccagagcag gnggagagag agcaaatttg g 351

<210> 215
<211> 1087
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1075)
<223> n equals a,t,g, or c

<400> 215
gctggagtcc cagtccaccc gccacgcccg agcagggcct gtccgccttc tacctctcct 60
actttgacat gctgtaccct gaggacagca gctgggcagc caaggcccct ggggccagca 120
gtcgggagga gccacctgag gagcctgagc agtgcccggt cattgacagc caagccccag 180
cgggcagcct ggacttggtg cccggcgggc tgaccttgga ggagcactcg ctggagcagg 240
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acatcaccgc agatcccatg gactggagcc ccagcaatgt gcagaagtgg ctcctgtgga 360
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caaccaactg cccaggggga tatgggtcct cttggggcct tcgggaccct ggggncaagg 1080
ggctttc 1087

<210> 216
<211> 1977
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1873)
<223> n equals a,t,g, or c

<400> 216
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aggaggaaga tgaggaagag gaggaagaag aggaggagga ggaggaagaa gagcctcagc 120
agcgagggca gggagagaag tcagccacgc cctcacggaa gattctggac cctaacactg 180
gggagccagc tcccgtgctg tcctccccac ctcctgcaga cgtctccacc ttcctggctt 240
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tggcgttcgt gaccaagccc aacagcgccc tggaatcctg ctccttcgcc cgccacagtc 660
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gtgagctggg gagggactcg gatgaactga ggcgcagcct acgccattgc cttggacagg 780
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ctggscacac ctnacccagc accctgcctt tgggctgcag ctcgcttggc ttctgcgttg 1920
ctccttcact atggaagcca cctcccttgg gatcctttgc tccactgcca catatgt 1977

<210> 217
<211> 2815
<212> DNA
<213> Homo sapiens

<400> 217
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gtcccggccg gccccgagca cccccgcgct gtcggtcccc cgctccggtc tttcgctttg 120
gcttccaact agttaaatgc ccttgagcgc gggtttccgc ggcccggctc ttcgcccccg 180
cggcgcgagt tgagccgttt ccccgcgctg tccgcgcggg cgctccgaca gcggctctgc 240
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tgtagctaca tagttatctg tgtacatcca cgctggggca tttttctcct gcttaatgag 360
gacttgactc gggagcaagt gtgaatcatt gccggggctg ggaaaggagg aaggcgcatt 420
taaccccctc ccaccccctct ccatgtccgt gtgtcactcg gctcggtcca cctggcgcgg 480
ccggtcctgg ggctgctgct gctgttgacg acgacgacga cgacgggggc tgcctctgct 540
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<210> 218
<211> 1645
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (347)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1643)
<223> n equals a,t,g, or c

<400> 218
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tgtccggctt tgctggccca gcaagcctga taagcatgaa gctcttatct ttggtggctg 120
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gcaaatgcat ctgtccacct tatagaaaca tcagtgggca catttacaac cagaatgtat 240
cccagaagga ctgcaactgc ctgcacgtgg tggagcccat gccagtgcct ggccatgacg 300
tggaggccta ctgcctgctg tgcgagtgca ggtacgagga gcgcagnacc accaccatca 360
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aatcaaggaa gccatcatta aattgtttta tttctctcaa aaaaaaaaaa aaaaaaccaa 1560
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aaaaaaaaaa aaaaaaaaaa aangg 1645

<210> 219
<211> 478
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (344)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (415)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (452)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (469)
<223> n equals a,t,g, or c

<400> 219
tcgacccacg cgtccgggga attcaaggag acgggggcga cgcggctgct ggcgcctcct 60
cgggtttggg gctgccgcca tcatgccggg gatagtggag ctgcctactc tggaggatct 120
gaaagtgcag gaggtgaaag tcagttcttc ggtgctcaaa gctgccgccc atcactatgg 180
agttcagtgt gacaagccca acaaggagtt catgctctgc cgctgggaag aaaaagaccc 240
ccggcggtgt ttagaggaag gcaagctcgt caacaaktgt gctctggayt tcttcaggca 300
gataaagctt tcactgtgca gagcctttta cagactattg gacntgcatc gactactccg 360
gcctgcagtg ttttcgtcgc tgccgcaaac agcaggccaa tttgacgatg tgtgngggc 420
aactgggatg gtgcggctga actggggaaa angttccagt caccaaatng aaaacagt 478

<210> 220
<211> 832
<212> DNA
<213> Homo sapiens

<400> 220
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cagcccctcc cttgtgtttc aaccaatcgg aagtgaattt aactagatgt agtaaccttt 180
tttttcttta cttctaaaaa agttacagtt tactaataaa gttaagtctg gttctgtcct 240
agaggaaata aattcactat taattcatgt cttaagttac ttgggttaaa acactttcag 300
ccacccagat taattaaagt ggagcagtgg agcccctggc tgggagatgg cctccagagg 360

agcagctgca gggcaygttc tgggcttagc gacagaggca agcaagggac tggtgtctct 420
ggtgagaggt gggtttgatg tatctctgtc ctatgctggt ctctcttctc ctttataaaa 480
tcctctgtgg tcaactgact actgcgtatc gcagtggaat aagactgcac agttgctggt 540
aggtgagttt aaagtcttaa tctatgcatt cagagaaata tttttatatg ctttgtgtaa 600
tttataacaa ggattttttt tttagctttg ttaactgtga attcacccct cctcctccac 660
tgcatattta aagcatgtgt tcacactgtg tgtaaacatt cactgaagat tttttctttg 720
tgcattgctg actgttcaaa cataacaagt attattaaaa ttaaatatta actgacaaaa 780
aaaaaaaaaa aaaactcgag ggggggcccg gtacccaatt cgcccggagt ag 832

<210> 221
<211> 1892
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1892)
<223> n equals a,t,g, or c

<400> 221
tgactctggg ctagagacct ccccaacaga gctgaggcca aggccgactc cccctctcaa 60
atggcgtggt ctgggcctat gacggcccct gcagtggagt ctgtactggc tgcgggggac 120
cctgctcatt tgaaaatctg acatcagctg ggcagtcgcc cccctcctcc tttcctccct 180
ctactctgac acagcactta gcacctgaat cttcgtttct ctcccaggga ccctccattt 240
tccatatcca ggaaaatgtg atgcgccaca ggtatcagcg tctggwtcgc cacttcacgt 300
tttagccaca agtgactcag tggaagatcc agagtcaaca gaggctcgtc aggaagatgt 360
ctacagaaaa ggtagaccaa aaggaggaag ctggggaaaa agaggtgtgc ggagaccaga 420
tcaaaggacc ggacaaagag gaggaaccac cagctgctgc atcccatggc caggggtggc 480
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aagtcttggc aggccgtgcc cgcagctgct gctgcagttt ggggtgctct tctgcaccat 660
cctccttttg ctctgggtgt ctgtcttcct ctatggctcc ttctactatt cctatatgcc 720
gacagtcagc cacctcagcc ctgtgcattt ctactacagg accgactgtg attcctccac 780
cacctcactc tgctccttcc ctgttgccaa tgtctcgctg actaagggtg gacgtgatcg 840
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cgtttttcct tcaataaact atttgtgtc agcttcaaaa aaaaaaaaaa aaaaaaaaaa 1860

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<210> 222
<211> 868
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (23)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (31)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (45)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (829)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (860)
<223> n equals a,t,g, or c

<400> 222
ntttcagcag ttccgcatgc ccntccgtgg naagcctgtt cgtgntattg ggcaagaacc 60
cccatgatgc ccaaggccat ccaagggcat ctgaagacca acccagctct ggaaaacctg 120
ttacttcata tccgggggaa tgtggctttg tgttcaccaa ggaggcctca cttgagatca 180
gggacatgct gctggccaat aaggtgccag ctgccgcccg tgctggtgcc atagccccat 240
gtgaggtcac tgtgccagcc cagaacactg gtctggggcc cgagaagacc tccttcttcc 300
aggctttagg catcaccact aaaatctcca gaggaaccat tgaaatcctg agtgatgtgc 360
agctgattaa gaccggagac aaagtgggag ccagtgaagc cacactgctg aacatgctga 420
acatctcccc cttctccttt gggctgatca tccagcaggt gtttgacaat ggcagcatct 480
acaaccctga agtgcttgac atcacagagg aaactctgca ttctcgcttc ctggagggtg 540
tccgcaatgt tgccagcgta tgtctgcaga taggttaccc aactgtggca tcagtgcccc 600
attctatcat caatggatac aagcgggtcc tggctttgtc tgtggagact gattacacct 660
ttccacttgc tgaaaaggtc aaggccttct tggctgatcc atctgcattt gtggctgctg 720
cccctgtggc cgctgccacc actgctgcac ctgctgctgc tgcagcccca gccaaagttg 780

aagcaaagga agagtcggag gaawcggatg agagkattkt camttcgana atcagcaaaa 840
gcaacaattc cagccagttn attgtgaa 868

<210> 223
<211> 1516
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1493)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1497)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1508)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1509)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1516)
<223> n equals a,t,g, or c

<400> 223
gaatgagcag gataactgtg tcctgattca tgatgtggac caaaggaaca gcgataaaga 60
tatctttggg gatgcctgtg ataactgcct gagtgtctta rataacgacc agaaagacac 120
cgatggggat ggaagaggag atgcctgtga tgatgacatg gatggagatg gaataaaaaa 180
cattctggac aactgcccaa aatttcccaa tcgtgaccaa cgggacaagg atggtgatgg 240
tgtgggggat gcctgtgaca gttgtcctga tgtcagcaac cctaaccagt ctgatgtgga 300
taatgatctg gttggggact cctgtgacac caatcaggac agtgatggag atgggcacca 360
ggacagcaca gacaactgcc ccaccgtcat taacagtgcc cagctggaca ccgataagga 420
tggaattggt gacgagtgtg atgatgatga tgacaatgat ggtatcccag acctggtgcc 480
ccctggacca gacaactgcc ggctggtccc caacccagcc caggaggata gcaacagcga 540
cggagtggga gacatctgtg agtctgactt tgaccaggac caggtcatcg atcggatcga 600
cgtctgccca gagaacgcag aggtcaccct gaccgacttc agggcttacc agaccgtggt 660
cctggatcct gaaggggatg cccagatcga tcccaactgg gtggtcctga accagggcat 720
ggagattgta cagaccatga acagtgatcc tggcctggca gtggggtaca cagcttttaa 780
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gcagacatat tggcaagcca ccccattccg agcagttgca gaacctggca ttcagctcaa 960
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gggcccgnnc caattn 1516

<210> 224
<211> 1306
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (148)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (887)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1242)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1264)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1303)
<223> n equals a,t,g, or c

<400> 224
gtccgcgcgg gcctcggacc tgggggcccc ccggacgtgg acgggggcgg cggcggggcc 60
ccggactccg tcggcgcaca tccccgtccc agcgcagaga gccaccccag gaaaagcccg 120
gctggacgag gtcatggctg ccgctgcnst tacaagcctg tccaccagcc ctctccttct 180
gggggcccca gttgcagcct tcagcccaga gcctggcctg gagccctgga aggaggccct 240
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ggccagtgac cagtcctctc cgtccacccc gtcaccccca ctgccccccg aggcagccca 360
ctttctgttt ggggagccca ccctgagaaa aaggaagagc ccggcccagg tcatgttcca 420
gtgtctgtgg aagagctgcg ggaaggtgct gagcacggcg tcggcgatgc agagacacat 480
ccgcctggtg cacctgggga ggcaggcaga gcctgatcag agtgatggtg aggaggactt 540
ctactacaca gagctggatg ttggtgtgga cacgctgacc gacgggctgt ccagcctgac 600

tccagtgtcc cccacggcct ccatgccgcc tgccttcccc cgcctggagc tgccagagct 660
gctggagccc ccagccctgc ctagtcccct gcggccgcct gccccgcccc tgcccccgcc 720
ccctgtcctg agcaccgttg ctaaccccca gtcctgtcac agtgaccgtg tctaccaggg 780
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<210> 225
<211> 584
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (486)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (542)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (562)
<223> n equals a,t,g, or c

<400> 225
tcgacccacg cgtccggcgt cctctcggag cccgtgcggt cacttagcca agatgcctga 60
ggaaacccag acccaagacc aaccgatgga ggaggaggag gttgagacgt tcgcctttca 120
ggcagaaaty gcscagttga tgtcrytgat catcaayacy ttctactcga acaargagat 180
cttcttgcgg gactgatctc caactcgtcc gacgctcygg acaaaatccg atacgagagc 240
ctgaccgacc ccagcaagct cgactcgggg aaggagctgc acattaacct catcccgaac 300
aagcaggacc ggaccctcac catcgtggga taccgggatc gcatgaccaa ggccgacctg 360
atcaacaacc tgggcaccat cgccaaktcg gggaccaaag cgttcatgga agytctgcag 420
gcgggcgcag atatttcyat gattggccag ttcggggtcg ggttctattc ggcctacttg 480
gtggcnagaa ggtgacggtg atcaccaagc acaacgatga cgagcattac gcctgggagt 540
cntccgcagg ggctcgttca angttccgca ttgacacagt gaac 584

<210> 226
<211> 523
<212> DNA
<213> Homo sapiens

<220>

<221> misc feature
<222> (34)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (498)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (514)
<223> n equals a,t,g, or c

<400> 226
tcgacccacg cgtccgccag cagaaggctg ttgngggacg tctgccagga ctgcatccag 60
atggtgacag acatccagac tgctgtaagg accaactcca cctttgttga agctttggtg 120
gaccatgcca aagcacagtg tgatctcctg ggcccggca tggctgacat gtgcaagaac 180
tatatcaacc agtattcgga cattgccgtc cagatgatga tgcacatgca acccaaagag 240
atctgtggcc tggttgggtt ctgcgaccaa gtgaaggaga tgcccatgca gactctgatc 300
cctgccaaag cggtctcaga gaacgtcatc cctgcattgg aactggtgga gcccattaag 360
aaggacacgg tccaggcaaa gaccagtgtt agctgtggag atatgcgagt tacgtggttg 420
aaggaagtgg ccaagctcca ttggacaaca acaggactga ggaagaaata gtttcaggct 480
tggataaatg tgctccantt gccctaagtc ctanctgaac atg 523

<210> 227
<211> 2377
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2369)
<223> n equals a,t,g, or c

<400> 227
gccgatcccg gagtcggagc cgttccaggt ctcgcagccg atctcgctac agccgctcga 60
agtctcggtc ccgcactcgt tctcgatctc ggtcgacctc caagtccaga tccgcacgaa 120
ggtccaagtc caagtcctcg tcggtctcca gatctcgttc gcggtccagg tcccggtctc 180
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gtccccccaa gtctcctgaa gaggaaggag cggtgtcctc ttaagaaaat ggtaatgtct 300
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gggagtaata ctgaagagag gggtctgcag aaaggatgtg tatgaagctt agataataat 480
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tccaacgtct gcattttccc cctttaaagc tgcggtctcc tgtttgataa aagaatattg 600
gccagtattg cagattttaa ctgatttggc tgatcctcca gggaccagtt tctgtgggcg 660
tgtattggar caggtttgtc tttaaatgtt aaagatgcac tatcctctta gagaaacaat 720
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aagggcccta agtagctcag atattaaagt agtattctca attaccaaat gtttcatttg 960
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tgtaagtact tataacatgg tgtatctttt tgcttatgaa tattctgtat tataaccatt 2280
gtttctgtag tttaattaaa acattttctt ggtgttagct tttctcagaa aaaaaaaaaa 2340
aaaaaaaaaa aaaaaaaaaa aaaaaaaang aaaaaag 2377

<210> 228
<211> 463
<212> DNA
<213> Homo sapiens

<400> 228
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ttgcttggcc attgagattt cgcatcctgc atgaaattgc ccttggtgta aattacctgc 120
acaatatgac tcctccttta cttcatcatg acttgaagac tcagaatatc ttattggaca 180
atgaatttca tgttaagatt gcagattttg gtttatcaaa gtggcgcatg atgtccctct 240
cacagtcacg aagtagcaaa tctgcaccag aaggagggac aattatctat atgccacctg 300
aaaactatga acctggacaa aaatcaaggg ccagtatcaa gcacgatata tatagctatg 360
cagttatcac atgggaagtg ktatccagaa aacagccttt tgaagatgtc accaatcctt 420
tgcagataat gtatagtgtg tcacaaggac attggactgg tat 463

<210> 229
<211> 1232
<212> DNA
<213> Homo sapiens

<400> 229
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caggtttttc cgccaactag accgggacgg gagcagatcc ctggacgctg atgagttccg 240

gcagggtctg gccaaactcg ggctggtgct ggaccaggcg gaggcagagg gtgtgtgcag 300
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gccccccatg tcccaggccc gggaggctgt catcgcagct gcatttgcca agctggaccg 420
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cttcgactcc tctgagaagg acgggcaggt cacactggcg gaattccagg actactacag 600
cggcgtgagt gcctccatga acacggatga ggagttcgtg gccatgatga ccagtgcctg 660
gcagctgtga gcagctccgg ctcagccctg ctgccctggc ctgtcactyc ccacccctgc 720
cggagacctc ccttccctgg gccccttctc ttctgggcag scacaccaca gagcggggag 780
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ctctccccac ccacgccatg ctgaccagag gtcttgcagc ccctgtggat gcccccgccg 960
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gacctgccca ggtgtggagc gaggggcaca ggggcatcct aacctcagaa actgaaataa 1140
agcctttgaa aaaaaaatct gtaaaacatc aacccccaat cagaagatgg caaatgggga 1200
ataaaaatag caggtaacac gtcaaaaaaa aa 1232

<210> 230
<211> 1063
<212> DNA
<213> Homo sapiens

<400> 230
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tcggtcagcc aacgcagagg atgctcagga attcagtgat gtggagaggg ccattgagac 180
cctcatcaag aactttcacc agtactccgt ggagggtggg aaggagacgc tgacccccttc 240
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<210> 231
<211> 1063
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1056)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1061)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1063)
<223> n equals a,t,g, or c

<400> 231
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cctcagctgc agcccggcag cgcattccta cccagggtcc gccgccagag ctttcccgcg 360
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gcttccgcca cactcatcat ggcggtggca gtaagtcact tccgcccggg accggaartg 480
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ctggccatag ggattggaac cctgatctac gggcactgga gcataatgaa gtggaaccgt 660
gagcgcaggc gcctacaaat cgaggacttc gaggctcgca tcgcgctgtt gccactgtta 720
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaanaaaa nan 1063

<210> 232
<211> 1474
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1337)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1359)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1377)
<223> n equals a,t,g, or c

<400> 232
ggattcctac cctcatcacg gcctttgtcc ttgctacctc tcaggcccaa gctggatggc 60
tgcaacatga ttatggccac ctgtctgtct acagaaaacc caagtggaac caccttgtcc 120
acaaattcgt cattggccac ttaaagggtg cctctgccaa ctggtggaat catcgccact 180
tccagcacca cgccaagcct aacatcttcc acaaggatcc cgatgtgaac atgctgcacg 240
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<210> 233
<211> 1782
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (31)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (34)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (591)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1760)
<223> n equals a,t,g, or c

<400> 233
aagatganag gctcacccta aaacatcttc nttnctctac cagtgagact atcaaccatg 60
gatctatcta tctatttttt aagcctgcat cacttcttga gataatgagg tttctacctc 120
caaagcctgc tgggtgagca ccttgctcat tatactggwt ctgaatttac ctctttgaag 180
tttctagatg caccacttcc tgctcacagc ctggaattcg gttaacaagt cagtgtcaac 240
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gccttatgga gaagtatgtt tctgctttct ttcctgrgga agcctagytt ctgggccacg 540
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<210> 234
<211> 2208
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1314)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (2189)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2202)
<223> n equals a,t,g, or c

<400> 234
acagggctcg gagccaagct cagagaacgc caatgacacc atcattttgc gcaacctgaa 60
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<210> 235
<211> 2580
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2558)
<223> n equals a,t,g, or c

<400> 235
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<210> 236
<211> 3008
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (3001)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3008)
<223> n equals a,t,g, or c

<400> 236
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ngggggggn 3008

<210> 237
<211> 877
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (834)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (854)
<223> n equals a,t,g, or c

<400> 237
caattattga agtcaagtga tgggcacaga ggattgatag ctcaaataag gcttggtact 60
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ttataatatg atgtaagtac agagagctgt gggaacataa aggaaggaaa atgaacttga 180
gtctgagact gctcacttct attagagccc tcttctgttt tgcttcatgt tcagccttca 240
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gtgacgtaca gctacatatt tttcctcaaa attgaggtga aaggaatttc taaagtaggc 360
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tggccctcta cttcagatta ctttctatga agacaaaaat tttcaaggcc gtcgctatga 480

ctgtgattgc gactgtgcag atytccacac atacctaagt cgctgcaact ccattaaagt 540
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<210> 238
<211> 3039
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (170)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (177)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3039)
<223> n equals a,t,g, or c

<400> 238
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tggtcatcag ccaggggaag attgtcctgg aggacggcac cctgcatgtn accgaangct 180
ctggacgcta cattccccgg aagcccttcc ctgattttkt ttacaagcgt atcaaggcaa 240
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aagtgtctgt gacgcccaag acagtcactc cagcctcctc ggccaagacg tctcctgcca 360
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<210> 239
<211> 1992
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (12)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (13)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (29)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (87)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1989)
<223> n equals a,t,g, or c

<400> 239
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ctagaactag tggatccccc gggctgnagg aattcggcac gagcgcggtg ctgctgcgcc 120
tgggcgatga gctggagatg atccggccca gcgtctaccg caacgtggcg cgtcagctgc 180
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tggccgtgga ctgtgtgagg caggcccagc ctgccatggt ccacgccctc gtggactgcc 360
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atgtcctcaa gtgtgtggtc agcacagacc ctggcctccg ctcccactgg ctggtggctg 480
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ggggtgggcc atgtgccagg acaggagggt cccggcggaa agccagcccc ggactcatcg 1860
tgacattgag atcccactgg agggtagggg tggtaataaa cttctccaaa cgatgcgttg 1920
tcattttaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980
aaaaaaaanc cc 1992

<210> 240

<211> 497
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (387)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (476)
<223> n equals a,t,g, or c

<400> 240
ggcagaactg tctgggacag acgctgcccg gatccctgcg gctgcctgca ctctggacca 60
cgagctctga gagcagcagg ttgagggccg gtgggcagca gctcggaggc tccgcgaggt 120
gcaggagacg caggcatggc cggtgagctg actcctgagg aggaggccca gtacaaaaag 180
gctttctccg cggttgacac ggatggaaac ggcaccatca atgcccagga gctgggcgcg 240
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gttgacrgcg acggcgacgg cgaaatcagc ttccaggagt tcctgacggc ggcrargaag 360
gccagggccg gcctggagga cctgcangtc gccttccgcg ccttcgacca ggatggcgac 420
ggccacatca ccgtggacga gctcaggcgg gccatkgcgg ggytggggma ccttcnagag 480
attgaccatt ttggagc 497

<210> 241
<211> 316
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (133)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (311)
<223> n equals a,t,g, or c

<400> 241
atcgggcagc ccacacaagc ggcaaaccag aatggcactg gaaatggagc cgcagaggta 60
cgcgatgagg atcattccag gcgcgattgc actcataagc tgttccgttt tgaaaattcg 120
tgttcaacga tgnaatctgt ggataatacg cacatttcgc cggaagtggt atccggttag 180
ccaraaagca ggcaggacgt gatggatatt gtatttatag agcaactttc ggtaatcacc 240
actattggtg tttacgactg ggrrcaacya tcgaacagaa gttagtgttc gatatcgaaa 300
tggcgtgggg ntaacc 316

<210> 242
<211> 829
<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (4)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (14)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (47)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (793)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (809)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (814)
<223> n equals a,t,g, or c

<400> 242
ngnntttctt cggngggggg gaataagggg acacagctca cactatntta aggtacgcct 60
gcaggtaccg gtccggaatt cccgggtcga cccacgcgtc cggaaagaaa agaagaaaag 120
aaaaaaagat ccttcaaagg gcagatgggt agaaggcata acctctgagg gttaccatta 180
ctattatgat cttatctcag gagcatctca gtgggagaaa cctgaaggat ttcaaggaga 240
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aacagtgagc cgagattgca ccaccgcact ccagcctgga taacaaagta agactccgtc 720
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<210> 243
<211> 838
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (32)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (51)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (822)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (832)
<223> n equals a,t,g, or c

<400> 243
taaacccgaa gtgccaaata ataatttaaa anatgttaat ttttttggcc ncctaaattt 60
gccctttcca tccattaaaa atgtccaagt tccaagtgat atgtgcccct aatatccacc 120
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gtacttgaat agttacagca tatgtttgaa caggaagtag gaacatgcat acacgaagaa 240
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tacactgctt ataatactaa tgtttacaga tatgtttctg tttataacca tataatacat 720
tggctttgtc atattagttt tttttgcaag tagttatgta aaagagatag ataataaaat 780
attaaataac aaaaaaaaaa raaaargctc gagtaarggc anagtggcat gngccata 838

<210> 244
<211> 2853
<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (2665)
<223> n equals a,t,g, or c

<400> 244
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cgctaaccgg ggaggggggc cggtaggggc gcctcgggty tcaaggcgcc gggagggtct 2760
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<210> 245
<211> 1197
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (218)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1193)
<223> n equals a,t,g, or c

<400> 245
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cacatcaaac tgaccgactt trgactctgc aaggagtcta tccatgaggg cgccgtcact 180
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gccggtggac agtcctgatg acacagccct cagcgagagt gccaaccagg ccttcctggg 660
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<210> 246
<211> 848
<212> DNA
<213> Homo sapiens

<400> 246
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ggcgtgttcg cgcaggctga cggctcggcc tacattgagc agggcaacac caaggcactg 180
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aaaaaaaa 848

<210> 247
<211> 1336
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (26)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1336)
<223> n equals a,t,g, or c

<400> 247
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gaagatgaag aagatgatgt gtcagagggc tctgaagtgc ccgagagtga ccgtcctgca 180
ggtgcccagc accaccagct taacggcgag cggggacctc agagtgccaa ggagagggtc 240
aaggagtgga ccccctgcgg accgcaccag ggccaggatg aagggcgggg gccagccccg 300
ggcagcggca cccgccaggt gttctccatg gcagccatga acaaggaagg gggaacagct 360
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ktttttttaaa taaaatttta aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1320
aaaaaaaaaa aaaaan 1336

<210> 248
<211> 1076
<212> DNA
<213> Homo sapiens

<400> 248
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tgtcgccatc gacatgatgg actctcggac cagccagcag ctgcagctca ttgacgagca 180
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<210> 249
<211> 2425
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (52)
<223> n equals a,t,g, or c

<400> 249
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accagtggcc atggttgcca gccttgtgcc tgccacccaa gccgggccag aggccmwcct 180
gcaacgagtt cacagggcag tgccactgcs gtgccggctt tggagggcgg acttgttctg 240
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aaaaaaaaaa aaaaaagaaa aaaaa 2425

<210> 250
<211> 1408
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (252)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1387)
<223> n equals a,t,g, or c

<400> 250
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cgagcccgag ctggccgtgt cagcgccggg ccgcgtgcaa cctcatcggg gaacacacgg 180
actacaacca gggcctggtg ctgcctatgg ctctggagct catgacggtg ctggtgggca 240
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gtgcagtggt ggtcagctca gtgcccctgg ggggtggcct gtccagctca gcatccttgg 480
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aaaaaanaaa aagaaaaaaa aaaaaaaa 1408

<210> 251
<211> 494
<212> DNA
<213> Homo sapiens

<400> 251
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gccagccaag gacagggtgg actgcggcta cccccatgtc acccccaagg agtgcaacaa 180
ccggggctgc tgctttgact ccaggatccc tggagtgcct tggtgtttca agcccctgca 240
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cggagcaccc ttgcccggct gtgattgctg ccaggcactg ttcatctcag cttttctgtc 360
cctttgctcc cggcaagcgc ttctgctgaa agttcatatc tggagcctga tgtcttaacg 420
aataaaggtc ccatgctcca cccgaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480
aaaaaaaaaa aagg 494

<210> 252
<211> 2491
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (16)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2457)
<223> n equals a,t,g, or c

<400> 252
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acgggtcccg acgcgacagt gggcgggcca gcgccgaccc cgctgctgcc cccctcggcc 120
acagcctcgg tcaagatgga gccagagaac aagtacctgc ccgaactcat ggccgagaag 180
gactcgctcg acccgtcctt cactcacgcc atgcagctgc tgacggcaga aattgagaag 240
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aagaacatga aactgaaaga gcgagtgctg atacctgtca agcagtatcc caagttcaat 360
tttgtgggga agattcttgg accacaaggg aatacaatca aaagactgca ggaagagact 420
ggtgcaaaga tctctgtatt gggaaagggc tcaatgagag acaaagccaa ggaggaagag 480
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<210> 253
<211> 1125

<212> DNA
<213> Homo sapiens

<400> 253
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cgagatattt ttgggagtta ttccctaaat aactgcatta tatgctcctt tcatgacgaa 120
attgctgccg tggagaagac tggaggaaac tcgaggaaga gggagaagcc gacaagtgct 180
cgacgggcta ggaactgtcc tgcttgggtg ttagcgtttc ccgycgggcc agtaaggctg 240
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agacacattg cattttctgg aaacaaatgg gaacaaaaag tatactcttc gcatactggc 540
tacccaggtg gatttagaca agtaacagct gctcagcttc acctgaggga tccagtggca 600
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gaaaggttgc atctttttcc agatgagtat attccagaag atattcttaa gaatttagta 720
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<212> DNA
<213> Homo sapiens

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<211> 490
<212> DNA
<213> Homo sapiens

<400> 255
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tcgccgccca ggccgcctgg gttccacttc cagcaacagc tcctgcagca gtaccgagtg 180
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agccccgagg aagcagcccg gcggtcagtc cagcamagcc agcgctgggc ccccgtcctg 420
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gggccctttg 490

<210> 256
<211> 1233
<212> DNA
<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (602)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (931)
<223> n equals a,t,g, or c

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ggagccctgc cctgaggatt acaagtacat ctcagagaac tgcgagacgt ccaccatgaa 120
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<210> 257
<211> 2404
<212> DNA
<213> Homo sapiens

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<222> (2372)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2385)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2395)
<223> n equals a,t,g, or c

<400> 257
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<211> 2092
<212> DNA
<213> Homo sapiens

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<222> (4)
<223> n equals a,t,g, or c

<220>
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<222> (27)
<223> n equals a,t,g, or c

<220>
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<222> (31)
<223> n equals a,t,g, or c

<220>
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<222> (60)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (2069)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2071)
<223> n equals a,t,g, or c

<400> 258
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<210> 259
<211> 387
<212> DNA
<213> Homo sapiens

<220>

<221> misc feature
<222> (377)
<223> n equals a,t,g, or c

<400> 259
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actgaaaaaa aaaaacnggg ggggccg 387

<210> 260
<211> 3712
<212> DNA
<213> Homo sapiens

<400> 260
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<211> 897
<212> DNA
<213> Homo sapiens

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<222> (22)
<223> n equals a,t,g, or c

<400> 261
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aacccggact tgtactcggg gccgtgggct cggcccggac ccggcattcg gacttggact 780
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<210> 262
<211> 1905
<212> DNA
<213> Homo sapiens

<220>
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<222> (1266)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1791)
<223> n equals a,t,g, or c

<400> 262
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<210> 263
<211> 1424
<212> DNA
<213> Homo sapiens

<400> 263

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gtgactgttt gattttaaaa agtgtgactg tcagttgtat ctgttgcttt tctcaatgat 180
tcagggatac aaatgggctt ctctcattca ttaaaagaaa acgcgacatc tttctaagat 240
tctctgtggg aaaatgactg tcaataaaat gcgggtttct gggccattcg tcttactttc 300
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gtaaaagtcc caggttctaa attaactaaa tgtgtacaga aatgaacgtg taagtaatgt 480
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<210> 264
<211> 1287
<212> DNA
<213> Homo sapiens

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<222> (111)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (889)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1196)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1229)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1284)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1287)
<223> n equals a,t,g, or c

<400> 264
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ccgtcccgcg gcccccagcc gcccccaacc ctgccccacg ggcccggcgc catgagtgag 180
ctggagcaac tgagacagga ggccgagcag ctccggaacc agatccggga tgcccgaaaa 240
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cagatgagga cccggaggac cctccgtggg cacctggcaa agatctatgc catgcactgg 360
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gtggggatgt gatgtccctg tccctggccc ccgatggccg cacgtttgtg tcaggcgcct 780
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<210> 265
<211> 991
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature

<222> (421)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (966)
<223> n equals a,t,g, or c

<400> 265
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ccctggagct cttccgaacc aaggtgaatg cgctcactta tggggaggtg ctgcggctgc 180
ggcagactga acggctgcac caggagggca cactggctcc ccctatactg gagctgcggg 240
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<210> 266
<211> 2320
<212> DNA
<213> Homo sapiens

<400> 266
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tccagaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2320

<210> 267
<211> 423
<212> DNA
<213> Homo sapiens

<400> 267
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tgggctcaaa gtctgcctgc aagcggctct gagggcttgg aatagctgca atgagtacat 360
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act 423

<210> 268
<211> 1846
<212> DNA
<213> Homo sapiens

<220>
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<222> (1776)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1816)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1832)
<223> n equals a,t,g, or c

<400> 268
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aaagctgatc ttttcnggat ataaaatgtt gnatgatgaa aaaaaa 1846

<210> 269
<211> 601
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (536)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (556)
<223> n equals a,t,g, or c

<400> 269
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gtctcatact ctacaccagt attgctgtcc tactcaggtc cttgactcca tgaagcttac 180
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tccttccccc cacccacccc cccgcagatt cccccatggg accctgtccc ctgcttcagg 420
aaccagatgg gcaagcatcg tgccccttcc tccccccacc ttcttcttgg aattcccatc 480
cccactgctg tctcctctgg actccagccc ctgaattaaa gaaactggag ccctangtcc 540
gactaaaatt tgggganaagc aaacttggac ttggacttgg aactggatcc tcccgtaccc 600
g 601

<210> 270
<211> 880
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (876)
<223> n equals a,t,g, or c

<400> 270
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aatctattct gtatccacca ggtggcagca tcttgtcata cgtgtcagga cttaggactg 480
cggggtttag gttagatgtc acggaaaaag ctagttctgt ggtcaggcgg caccaatgag 540
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ttgaagacct actttgtcct ctacataggg tagcttctgt cagggaatct tggttcttcc 660
caagaaacac tgattttctt tcagggagac ttcatgtgtt catttatttc caccacagca 720
gattttaaga aattataata tgtaatattt gatatctata aagagtatat ctaacgtgaa 780
taaattatga agcatactaa tgagtaccta tgacccataa cacatataca ttaaaacatt 840
ttaaatacca aaaaaaaaaa aaaaaaaaaa aaaaanaaaa 880

<210> 271
<211> 2484
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (194)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (623)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2396)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2484)
<223> n equals a,t,g, or c

<400> 271
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cgatcaagtt ccttcccatt tctccatctg gggatcctg aacgtgcaca tcctcagaga 180
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ccgtgccggg cctgcctacc actagatccc cacccaccta tgactgctca gtcccgctct 420
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caaactccaa ggctgggcaa ggcactgatc cactgctgga cagacccggg gcagcctctg 540
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gggccagggc caggactcag ccagtcccat ccggaccaca cacacggggc aggtgctggg 720
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tgttttcaga agtttctttg gggcaacta cattaaattc actgaggaag aggagcagct 2040
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gcctgcggtg ggccgggctc tgaaggccca caggctccag ttctggaaga aggcgctgcc 2220
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gccggggagg agggggtggg ttcgctgaca ggcgagggtc agcctgctgt gcccacacac 2340
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gtccatccat tcagaaagcw tttatttaag attttayttc agggmtwgat kggcccatat 2460
tgttaatttc cccgtttttt gggn 2484

<210> 272
<211> 751
<212> DNA
<213> Homo sapiens

<400> 272
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ccactcaccg aggcactgag ggctctctgc cacgtggggc tctttractt cgccttttgt 120
gccttgtttg actgcraccg ccctgtggsg cagaagtctt gtgacctcct tctcttcctg 180
agggacaaga ttgcttccta cagcagcctg cgggaggcca ggggcagccc caacactgcc 240
tccgcagagg ccamcctgcc gaggtggcgg gcgggtgagc aggcccagcc cccaggggac 300
caggagcctg aggctgtgct ggccatgctc aggtccctag acctggaggg cctgcggagc 360
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caaggtcaag aaatcccaca gtttgatgta ttaaagaaat gacttatttc tactcaaaat 660
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acaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 751

<210> 273
<211> 3309
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (3279)
<223> n equals a,t,g, or c

<400> 273
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gccagggtag aaaccaaggg gtcagggctg ggctggagga cacggctgag gtcctcccaa 120
aactgggccr atgtggtgtg acatccccac cagcctcaga tgagacgggc caggacgccc 180
agccacagca agccctgtcc ctttgccgga tccccaaaca ctagagaagc tctcctaacc 240
caaggcggag aatgaaggtg gtggcggcag aggaggaggg cagcagctga gaggccaggg 300
acagggtgcc tcgccaagct gtctgaggtc tgtcccaggt ggcccaggtg gtgcaggtag 360
aacagggtga ggagaggggg tcggctcarc aggaggaggc tgtggctgca gagcctggrg 420
gagcttttag gtgttgagat ggggcagctc tgaatcctag accctggaat agcctgtccc 480
ttttctctgg gtctcgtggt ggagccatga tctgggctgc tctcttgggg acactgggtg 540
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cttgctgggg tcccctcatc cacttgaggg cgcctgaggg ccaggarcag caggcaagga 660
gcctgggtct aggctaaggg ggtktktgcy cacctcctcc ctgaccctta acactcctgt 720
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gctgcagcct ttccgcactc tgagaccatg atcttcctcc tgccagggga gagccaccca 840
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ctccacttgg ggaccctgcc tcgtgtcgtc tttatctgcc tattactcag cctaaggaaa 3180
caagtacact ccacacatgc ataaaggaaa tcaaatgtta tttttaagaa aatggaaaat 3240
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ttcgcctaa 3309

<210> 274
<211> 843
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (780)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (833)
<223> n equals a,t,g, or c

<400> 274
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ccgtccacag ctcacgacca gatgcaccag caggagtcca catcgaggac gtcctccggg 120
cactcccacg accagtgacc aggagttaaa ctttgggatg tgcccgtgat gttggaccac 180
aaggacttag aggccgaaat ccaccccttg aaaaatgaag aaagaaaatc gcaggaaaat 240
ctgggaaatc catcaaaaaa tgaggataay gtgaaaagcg cgcctccaca gtcccggctc 300
tcccggtgcc gagcggcggc gtttttttctt tcattgtttc tctgcctttt tgtggtgttc 360
gtcgtctcat tcgtcatccc gtgtccagac cggccggcgt cacagcgaat gtggaggata 420
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tgtgtggacg aaggcttttc ctctccctgc acctttgcag ctgctgtgtc gggggccaac 600
gcagcacgct ctgggagwga cctgtggccc aagacgtggc cctcgtggag tgtgctgtgc 660
cccagccaag aggcagtgag gcaccttctg cctgcatcct ggtgggcaga cccagttctt 720
tcattgcagt caacttgttc acaggggaaa ccttggaaac cacagccagc agttcagggn 780
gaatggtcca tctgagcctt ttgtgcagtt gctgatgtgg agttcgatgg ggncccaaac 840
tgt 843

<210> 275
<211> 2028
<212> DNA
<213> Homo sapiens

<400> 275
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ttgaacctct ttatagcatt gatactaggt gaacagaaat tacctgacta ataatttgtc 180
taacatcata tatcagaatt ttattgtata tgatgaacaa aacttaaaat tttttaaatt 240
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taaaaactgt aagaataatt tagcagaaat agaaccagaa tgtagaagag tagtcatgta 360
acagcagtaa taacatactt cagcttccat ataggaatag aagtggtaga gccaaaagtg 420
atttaggaaa agttataagg tacaggttga gtatcccttt tccaaaaatg cttgggacaa 480
gaagtatttc agatttcata attttttttca aagtttggaa tatttgcatt atacttacca 540
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ttggcactca aaaaggttca acattgagtc cacttaacac ttaggtgtta gaagacctaa 660
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ggaagttagt ctaataattc actgcagaaa attgattaag tggctgtcct tttaattaag 840
agtgtggagt cataaactta agttcttcat atagtgacaa gagtccttag agattgttat 900
tcaagttcct tagaaattgt tatttaggta taatatcatc ttgtctttga ctagagcttg 960
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acaggatttt aaacatggtg tggtattcta aagccttttt tttaaaaaaa gagatctttt 1920
tgagagaaac aaatgaggat tgtaaagttt ggggacttac ctctgtagca ttgtgaaaat 1980
aaactttgat taagctgaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 2028

<210> 276
<211> 1455
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (759)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1408)
<223> n equals a,t,g, or c

<400> 276
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gcacccggtg gggcctyggc ggcacctgcg tcaacgtggg ctgcatcccc aagaagctga 300
tgcaccaggc ggcactgctg ggaggcctga tccaagatgc cccccaactat ggctgggarg 360
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aatccttgaa ctggggccac cgtgtccagc ttcaggacar aaaagtyaag tactttaaca 480
tcaaagccag ctttgttgac gagcacacgg tttgcggcgt tgcaaaggtg ggaaagagat 540
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catcgaaggt gccttggaat atggaatcac aagtgatgac atcttctggc tgaaggaatc 660
ccctggaaaa acgttggtgg tcggggccag ctatgtggcc tgggagtgtg ctggcttcct 720
caccgggatt gggctggaca ccaccatcat gatgcgcanc cscccctccgc ggcttcgacc 780
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ctggggacaa gtgtg 1455

<210> 277
<211> 1923
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1814)
<223> n equals a,t,g, or c.

<400> 277
ggccctgccc acccaggccg caagagctgc cgggacggtc cccatcttct tggagcgctt 60
taggctggcc ggcggcgctg ggaggtggag tcgttgctgt tgctgtttgt gagcctgtgg 120
cgcggcttct gtgggccgga accttaaaga tagccgcaat ggctgaaaat ggtgataatg 180
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ttgtggaagc attgagcaaa tccaaggcag aactcatgga aatcagtgaa gataaaacta 420
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taaaaaacag atctgtttat attaaaggct tcccaactga tgcaactctt gatgacataa 540
aagaatggtt agaagataaa ggtcaagtac taaatattca gatgagaaga acattgcata 600
aagcatttaa gggatcaatt tttgttgtgt ttgatagcat tgaatctgct aagaaatttg 660
tagagacccc tggccagaag tacaaagaaa cagacctgct aatacttttc aaggacgatt 720
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aacaggagca agaagcaaaa caaaagttag aagaagatgc tgaaatgaaa tctctagaag 840
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gaactagaat attagctatt gacgatgggc ctttcccaca ggccatttat ggtgtctcct 1800
aggctgggct ttgnatattt acacaggaaa gttgggtaac actagaaata attacttggt 1860

cacaaagcct tcccttttt tttccttttc gagactgagt ctcactccta tcgcgcagct 1920
gga 1923

<210> 278
<211> 1380
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1293)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1297)
<223> n equals a,t,g, or c

<400> 278
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cggaacgaca cacacacaca cacacacaca cacacacaca cactcgcata ctcatgcaca 120
ttttccttca tttccagatc ctttatttca gagcagccca ttttcctctg gattcattga 180
tgaatacaag tacccacacc tttggccagt aatgtcagtt acctgctgca ggttctgtgt 240
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cagactgggt tctagagagg cagagtcttt aagagtattc atttcttctg gaaggtggag 360
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<210> 279
<211> 1018
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (818)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1017)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1018)
<223> n equals a,t,g, or c

<400> 279
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ttcgcgctcg gcttgtcggg cgggagctcg tctcgatgct agcccgcgag ctacccgccg 180
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ttttcgacct gctgatcctg gggggtgggcc ccgatggtca cacctgctca ctcttcccag 480
accacccccct cctacaggag cgggagaaga ttgtggctcc catcagtgac tccccgaagc 540
caccgccaca gcgtgtgacc ctcacrctac ctgtcctgaa tgcagcacga actgtcatct 600
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ccagagggac gccgcagctg ggaccaggca cgcggccnat ggggctgggc ccctgctggc 840
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<210> 280
<211> 1192
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1105)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1130)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1154)
<223> n equals a,t,g, or c

<400> 280
tccgggaatt cccgggtcga cccacgcgtc cgctctgttt atatagcagg tgtcacaact 60
aacttgtctt tagccttggt gctttgatcc ttctatattt tgaccccaca ggtgtggtcc 120
ggtttactta atcaggacat gggcctaaga acaaaccttt tcccttcatg ataacatcca 180
tagacaactt attagaaggg actagagttt ttgcaaattt ccctgctgga tggggcctat 240
agctatactt agtatatgcc taaacatggt aattggatag taaatggttt tctagttcca 300
ttgctgtata tttgcctaaa tggacttgtg ttcaaattat ttcttcaatt gtcatagata 360
atcctgtacc aaatggggaa gaattaggaa ataatcatgt tgtctaatgg tactctggat 420
tcagggcagc aactgccatt taaatgttgt cttgttcatt tctaaatctg ttccatgaag 480
tttaggtttt ccctgaaact aagttgaatt atttccaaaa tgaaacaggc ttctcaggga 540
catatccact tcttcccagt ctgcctttgg attaaagcac caagcagaga ccacattaat 600
tccctttgct atactgtgat ccttagtatg ttaattctta agaaaccaac atatcactga 660
aagaaggctg gcagaacgca agtgcatttt ttcactgtgg gaagaaagat caagtgacgt 720
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cggtcttggt tctgccactc attggttatg aggaggccca gagcaggtaa gttcaccttc 840
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ttatttttaa atttttaata ctttnggtac tccaattgtc cagtgttccn tgggtgttgt 1140
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<210> 281
<211> 1755
<212> DNA
<213> Homo sapiens

<400> 281
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agtcgtctat aaaaactcat ctctgcgcgt ctcttcgcca cattcgcttc ctgctttcgg 180
tgtgtctgtt gtgtcttgtt gcgggcaccg cagtcgccgt gaagatggcg tctaccagcc 240
gtttggatgc tcttccaaga gtcacatgtc caaaccatcc agatgcgatt ttagtggagg 300
actacagagc cggtgatatg atctgtcctg aatgtggctt ggttgtaggt gaccgggtta 360
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caatgagcag ttctgatcgg gcaatgatga atgcattcaa agaaatcact accatggcag 600
acagaatcaa tctacctcga aatatagttg atcgaacaaa taatttattc aagcaagtat 660
atgaacagaa gagcctgaag ggaagagcta atgatgctat agcttctgct tgtctctata 720
ttgcctgtag acaagaaggg gttcctagga catttaaaga aatatgtgcc gtatcacgaa 780
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gacagtccta tagactgatc tatcctcgag ccccagatct gtttcctaca gacttcaaat 1140
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ttctaagtaa aaaaa 1755

<210> 282
<211> 1093
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (90)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (970)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1081)
<223> n equals a,t,g, or c

<400> 282
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gcctccgcgg atccgggccc gctcggcccn tcccatggaa ggtgctcggg tcttcggggc 120
actgggtccc atcggtccct cctcacctgg gctcaccctc gggggtctgg ccgtgagcga 180
gcaccggctc agcaacaagc tgctggcttg gagcggcgtc ctcgagtggc aggagaagcg 240
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gaaccaaggc gagaacctgg agaccgacca gtggccgcag aagctgatca tgcagctgat 360
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ccacttcacc aacagagact gcgactcgct caaggggctc tgccgcatca tgggcaacgg 480
cttcgcgggc tgcatgctgt tcccccacat ctccccctgt gaggtgcgcg tgctcatgct 540
cctgtactcg tccaagaaga agatcttcat gggcctcatc ccctacgacc agagcggctt 600
cgtcagtgcc atccggcagg tcatcaccac ccgcaagcag gcagtgggac ctggtggtgt 660
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gtggcaggag cccaggcctg agcccaacag tcggtccaag aggtggctgc catcccacgt 780
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gctcctgtac tcttcagaga agaaaatytt cattggcytc atccccccatg accagggcaa 1080
ntttgttcaa agg 1093

<210> 283
<211> 1556

<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1324)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1339)
<223> n equals a,t,g, or c

<400> 283
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agaaactgga cagttccgga cagcggwcaa ggcaaggawg tcatgcttga aggccagggt 120
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aaggtgaggg cttaggcagc tgtagaaccc caggaaagaa cggaatccag gcaatctgtt 540
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<210> 284
<211> 1029
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (828)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (958)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (972)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (976)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (987)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1007)
<223> n equals a,t,g, or c

<400> 284
tgatggtgtg gtccaatgag cgggtcatgg gttgggtgtc cgggctgggc tgaaggaatt 60
tgccacgaac ctcacggaga gcggggtaca cggggcactg ctcgccctgg acgagacctt 120
cgactactcc gacctggcct tgctcctgca gatccccacg cagaatgcac aggcccggca 180
gcttctggag aaggaattca gcaaccttat ctccttaggc acagacaggc ggctggacga 240
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cacatgaact ggactgagag ggggaagaag cggggaggaa gaaatcccgc cccaaacgtc 720
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ccgtgtttt 1029

<210> 285
<211> 1583
<212> DNA
<213> Homo sapiens

<220>

<221> misc feature
<222> (1411)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1531)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1557)
<223> n equals a,t,g, or c

<400> 285
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ggggtcttcc ctgactgcac accctgccac cagtgctttg ctctctggga tgtgatcatt 120
gccgagctga ccaacaggac acacagattc ctggagaaag ccaaggcctt gaagatcagt 180
ggtgtgatcg ggccttaccg tgagactgtg gactcggtgg agaggaaagt cagcgagata 240
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gaggaagcag agaaactgat taaagatgtt acagaaatga tggctcaagt agaagtgaaa 360
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gaagccgaaa gcctagacaa cactgtgaaa gaacttgctg aacaactgga atttatcaaa 480
aactcagata ttcggggtgc cttggatagc attaccaagt atttccagat gtctcttgag 540
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caagaggagc aggctcgcct ccttgatgaa ctggcaggca agctacaaag cctagacctt 720
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gggggaggcc gaatttttg gaa 1583

<210> 286
<211> 1177
<212> DNA
<213> Homo sapiens

<400> 286
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aagayatctc aaaatgttta ccaatgtttt aagaagcttt gtgtgatatt cttccaaatg 120

tagttaccaa atataatatg gtagaaaagg ctaaatcata cttaatgagc aaattgaagt 180
aagcttttaa agtatatttc tcttttggtg aaaggccaat ggagacattg tgaatttaag 240
tgaacatttg cctcaagatg ttaactataa acacactgca tacaattttc ttctgaataa 300
caaatgaatg cttattgctg catgatgtaa gcaaaagtca ttatttttcc tattcatttg 360
aaataagtta tggcttaaaa tgcttttgga gtttatttct caaaattaaa atctggtcac 420
atgagcttta gtttgttttc tggtttaaaa aataaaaagg tttctcttaa cagtatttcc 480
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aattacgaca ttttaagata tttcatagac aaaccaaaca aaaatatatg tttttacttt 660
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atattttgat aatattttta cagtgagctt tcccatgttt ttatgtctta agtttctttg 780
ctgcgtttat gtaggttgca caagaacttt tactcacttg taattgtgcc tcagactttt 840
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agctaatagt agtttacaga caattctgat gattatgatt tcatttggtt taactaagct 1020
gtactagttc atttcataag gaaatgatac tgtagacaaa tgtaaataaa gcctgtgagt 1080
caagcatcaa gtggtgtttg ttagaaataa actagagatt tttaaaaaaa aaaaaaaaaa 1140
aaaaaaaaaa aaaaaaaaaa acccccgggg ggggccc 1177

<210> 287
<211> 506
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (394)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (470)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (481)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (494)
<223> n equals a,t,g, or c

<400> 287
acaagtagct gcagtacggt acggaattac agggtagacc caagcgtacg taaaatttaa 60
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taggtgttcc ctagtgtttc ttaatttctt tttagaaagt gtatttttat tagtattttt 180
ccggtgaaca gaagatttgt ttggatttaa acatttacta agacagtacc tattaggaaa 240
accaaatatt gcaaatggtc aattcgattt taatttctca aaagatactc tgttatccag 300
aagattaaaa tgcctacatt gagtgcttaa aaaaaaaaaa acmactgtga tratktgagc 360

agaatggcca gtaagttaag ccttttttgga tccnggtaat ccagggtatc catttaccat 420
ggaaagggga ttccccaaac tactggccca gagggaagtt tggtttttttn aaatttaagg 480
nggggaaatt ttanccctat aaaatt 506

<210> 288
<211> 948
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (3)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (926)
<223> n equals a,t,g, or c

<400> 288
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tcggggaaat ccaccgtggg cgccctgctg gcatctgagc tgggatggaa attctatgat 120
gctgatgatt atcacccgga ggaaaatcga aggaagatgg gaaaaggcat accgctcaat 180
gaccaggacc ggattccatg gctctgtaac ttgcatgaca ttttactaag agatgtagcc 240
tcgggacagc gtgtggttct agcctgttca gccctgaaga aaacgtacag agacatatta 300
acacaaggaa aagatggtgt agctctgaag tgtgaggagt cgggaaagga agcaaagcag 360
gctgagatgc agctcctggt ggtccatctg agcgggtcgt ttgaggtcat ctctggacgc 420
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ctggagcccc cagcagctcc agaaaacttt atccaaataa gtgtggacaa aaatgtttca 540
gagataattg ctacaattat ggaaacccta aaaatgaaat gacaatgatt ttgtatcagt 600
ggtccaaaca gaactaagca taaatcattg tgccatccca aacctcgttc cagccgcctt 660
gcccatacta gattctaaat gtttctaaag gcaaacccca atgtgtcaag acagacttgt 720
ttaggtgtaa ttttaggaat tatgctggtt catcaggaag cagaggggga gttttaaaag 780
tcaagcttaa attgaagttt aaattcatct ataaccaaat caaatgatca gaggaaattc 840
tgtaatcaat gctggaaatc gttacattgt ttagaacatt cttgctcatg cctgtatttg 900
cacaaataaa tgaaacttcg ctgtcnaaaa aaaaaaaaaa aaaaaaa 948

<210> 289
<211> 1034
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (376)
<223> n equals a,t,g, or c

<400> 289
ggcacgagct cgtgccggtt tgacctggag catgggtcct ggaccaaatt gccccgcagc 60
ctgcgcatga gggataagag ggcagacttt gtggttgggt cccttggggg ccacattgtg 120
gccattgggg gccttggaaa ccagccatgt cctttgggct ctgtggagag ctttagcctt 180

gcacggcggc gctgggaggc attgcctgcc atgcccactg cccgctgctc ctgctctagt 240
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gtggaggcac tgtgtctgcg tgatggggtc tgaaggcttg gtgggagctg tccactggag 360
cagctcattg ccagangmrg ctatttctat ggctcctttt gctgctgagg acactcactg 420
tggctctgtg ggatgagaga ggcatggggg tgagcacttg aaacactgcc ttggggcctt 480
gggttagggg agcctttgtc tttagtgcag gacacacata tgcttacacc tacctttatc 540
accattcgtt catgaatcat gcctagctcc atccttgccc tgggacctac taggccttcc 600
atccaactgg gaaatgggga gaagcaaagc tggcctcatg ctcttcaggg tcagttccta 660
tctggagttg accaggccta ccccagttgc cattcctgaa aaatctcagc tgccaggctg 720
cctttagggt ccctgtagac ccaggagagt tgagagggtg ggggacacag agagaataga 780
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tcagcatcct catctataaa tggggatctc tgaaaccttc ctaccctacc tacctcacag 960
ggctgttgtg aggacccagg gagtttggat gtggaagtaa aagtgctgct aaaacctaaa 1020
aaaaaaaaaa aaaa 1034

<210> 290
<211> 3091
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (24)
<223> n equals a,t,g, or c

<400> 290
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taaaacaaat cccagcagta atacatttct taaacctcac agtgcatgat atatcttttc 120
attctgatcc tgtgtttgca aaaatataca catgtatatc atagttcctc actttttatt 180
catttgtttt cctattacct gtagtaaata tattagttag tacatggaat ttatagcatc 240
agctaccccc aggaacagca cctgacaggc gggggatttt ttttcaagtt gttctacatt 300
tgcataaatt atttctatta ttattcatgt atgttattta tttctgaatc acactagtcc 360
tgtgaaagta caactgcaag gcagaaagtg ttaggatttt gcatctaatg ttcattatca 420
tggtattgat ggacctaaga aaataaaaat tagactaagc ccccaaataa gctgcatgca 480
tttgtaacay gattagtaga tttgaatata tagatgtagt attttgggta tctaggtgtt 540
ttatcattat gtaaaggaat taaagtaaag gactttgtag ttgtttttat taaatatgca 600
tatagtagag tgcaaaaata tagcaaaaat aaaaactaaa ggtagaaaag cattttagat 660
atgccttaat ttagaaactg tgccaggtgg ccctcggaat agatgccagg cagagaccag 720
tgcctgggtg gtgcctcctc ttgtctgccc tcatgaagaa gcttccctca cgtgatgtag 780
tgccctcgta ggtgtcatgt ggagtagtgg gaacaggcag tactgttgag aggagagcag 840
tgtgagagtt tttctgtaga agcagaactg tcagcttgtg ccttgaggct tccagaacgt 900
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tccttctgac ttataataga aaatgttttg aaagtaaaaa aaaaaaaatc taatttggaa 1380
atttgacttg ttagtttctg tgtttgaaat catggttcta gaaatgtaga aattgtgtat 1440

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tattgctaca gaatgctctg ttttggtgct ttgagttctg cagacccaag aagcagtgtg 2040
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tgctcctttc ccaagaggca gatgaaaata tagccagttt atctataccc ttcctatctg 2460
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caaaacttta agtaccctat cattaaaaat ctggttttaa aagtagctca agtaagggat 2580
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agaatgaaaa tgtaggtatt tattgtcaga tgatgaagtt cattgttttt ttcaaaattg 2820
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aaagagcaaa tagtttgtat atttgtaata ccttttgtat ttcttacaat aaaaatattg 2940
gtagcaaata aaaataataa aaacaataac tttaaactgc tttctggaga tgaattactc 3000
tcctggctat tttcttttt actttaatgt aaaatgagta taactgtagt gagtaaaatt 3060
cattaaattc caagttttag caaaaaaaaa a 3091

<210> 291
<211> 518
<212> DNA
<213> Homo sapiens

<400> 291
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tgagtccagt tgagggggaa acagtaccag cactgcgggg catgaagaag agtgtggggc 120
tgccggtggc cgtgcagtgt gtggctctgc cctggcaaga agagttgtgt ctgcggttca 180
tgcgggaggt ggagcgactg atgacccctg aaaagcagtc atcctgatgg ctctggctcc 240
agaggacctg agactcacac tctctgcagc ccagcctagt cagggcacag ctgccctgct 300
gccacagcaa ggaaatgtcc tgcatggggc agaggcttcc gtgtcctctc ccccaacccc 360
ctgcaagaag cgccgactcc ctgagtctgg acctccatcc ctgctctggt cccctctctt 420
cgtcctgatc cctccacccc catgtggcag cccatgggta tgacatagcc aaggcccaac 480
taacagtcaa gaaacaaaaa aaaaaaaaaa aaaaattc 518

<210> 292
<211> 498
<212> DNA
<213> Homo sapiens

<220>

<221> misc feature
<222> (447)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (468)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (475)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (479)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (482)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (489)
<223> n equals a,t,g, or c

<400> 292
ctcgtgccga attcggcacg agcaacgtcg ctccagctgc tcttgacgac tccacagata 60
ccccgaagcc atggcaagca agggcttgca ggacctgaag caacaggtgg aggggaccgc 120
ccaggaagcc gtgtcagcgg ccggagcggc agctcagcaa gtggtggacc aggccacaga 180
ggcggggcag aaagccatgg accagctggc caagaccacc caggaaacca tcgacaagac 240
tgctaaccag gcctctgaca ccttctctgg gatcgggaaa aaattcggcc tcctgaaatg 300
acagcaggga gacttgggtc ggcctcctga aatgayagca gggagacttg ggtgaccccc 360
cttccaggcg ccatctagca cagcctggcc ctgatctccg ggcagccacc acctcctcgg 420
tctgccccct cattaaaatt cacgttncca aaaaaaaaaa raaagggngg ccgcntagng 480
gntccaagnt tagttacg 498

<210> 293
<211> 469
<212> DNA
<213> Homo sapiens

<400> 293
ggccagccct ggggcgcctt aaaaaccgga gctggcgctt ggcakcgcca ctctgggcag 60
gatccaacgt cgctccagct gctcttgacg actccacaga taccccgaag ccatggcaag 120
caagggcttg caggacctga agcaacaggt ggaggggacc gcccaggaag ccgccatgga 180
ccagctggcc aagaccaccc aggaaaccat cgacaagact gctaaccagg cctctgacac 240
cttctctggg atygggaaaa aattcggcct cctgaaatga cagcagggag acttgggtcg 300

gcctcctgaa atgayagcag ggagacttgg gtgaccccc ttccaggcgc catctagcac 360
agcctggccc tgatctccgg gcagccacca cctcctcggt ctgccccctc attaaaattc 420
acgttcccaa aaaaaaaaa aaaaaaaaag gggggcccg gtccccatt 469

<210> 294
<211> 668
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (568)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (650)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (652)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (658)
<223> n equals a,t,g, or c

<400> 294
gcacagaagg gggaggccaa agtgggtggg agcgcgtgct gttgggagtt gcttggaggt 60
tggcggcgcg gggctgaagg ctagcaaacc gagcgatcat gtcgcacaaa caaatttact 120
attcggacaa atacgacgac gaggagtttg agtatcgaca tgtcatgctg cccaaggaca 180
tagccaagct ggtccctaaa acccatctga tgtctgaatc tgaatggagg aatcttggcg 240
ttcagcagag tcagggatgg gtccattata tgatccatga accagaacct cacatcttgc 300
tgttccggcg cccactaccc aagaaaccaa agaaatgaag ctggcaagct acttttcagc 360
ctcaagcttt acacagctgt ccttacttcc taacatcttt ctgataacat tattatgttg 420
ccttcttgtt tctcactttg atatttaaaa gatgttcaat acactgtttg aatgtgctgg 480
taactgcttt gcttcttgag tagagccacc accaccatag cccagccaga tgagtgctct 540
gtggaccaca gcctaagctg agtgtgancc cagaagccac gatgtgctct gtatccagac 600
acacttggca gatggaggaa gcatctgatt gagacatggt gtacaggtcn gnaatgcngt 660
ttgttttc 668

<210> 295
<211> 1400
<212> DNA
<213> Homo sapiens

<400> 295
gctttgtcct ccagtggctg gtaggcagtg gctgggaggc agcggcccaa ttagtgtcgt 60
gcggcccgtg gcgaggcgag gtccggggag cgagcgagca agcaaggcgg gaggggtggc 120

cggagctgcg gcggctggca caggaggagg agcccgggcg ggcgaggggc ggccggagag 180
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gcgctagccg tggcaggagc agcccgcacg ccgcgctctc tccctgggcg acctgcagtt 300
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gtgggggatg ccctggagga agtgctcagc aaagccctga gtcagcgcac gatcactgtc 420
ggggtgtacg aagcggccaa gctgctcaac gtcgaccccg ataacgtggt gttgtgcctg 480
ytggcggcgg acgaggacga cgacagagat gtggctctgc agatccactt caccctgatc 540
caggcgtttt gctgcgagaa cgacatcaac atcctgcgcg tcacaacccg ggccggctgg 600
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cccggacctg cactgcgtgt ggtgacgaat ccacattcat ctcaatggaa ggatcctgcc 720
ttaagtcaac ttatttgttt ttgccgggaa agtcgctaca tggatcaatg ggttccagtg 780
attaatctcc ctgaacggtg atggcatctg aatgaaaata actgaaccaa attgcactga 840
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agatgacttt gcagatggaa agaggtgaaa atgaagaagg aagctgtgtt gaaacagaaa 1020
aataagtcaa aaggaacaaa aattacaaag aaccatgcag gaaggaaaac tatgtattaa 1080
tttagaatgg ttgagttaca ttaaaataaa ccaaatatgt taaagtttaa gtgtgcagcc 1140
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catatttgaa aaccatattt tattgtattt tgatgagata ttaaattctc aaagttttat 1260
tataaattct actaagttat tttatgacat gaaaagttat ttatgctata aattttttga 1320
aacacaatac ctacaataaa ctggtatgaa taattgcatc aaaaaaaaaa aagggggggcc 1380
gctcgcgatc tagaaactag 1400

<210> 296
<211> 960
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (599)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (859)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (933)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (950)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (951)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (959)
<223> n equals a,t,g, or c

<400> 296
gtcagcccga gcccgtgcrg gccctttaag ggccgggggc gtgtagcggg cccgccccct 60
ccccgcggcg cccgcagtcc gttaagtgcg agccccggcg caggggccgg atctggccgg 120
gggccggcgg cggtgtggga gcggcgcgtc atgtacacca tcaccaaggg gcccagcaag 180
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ctcctgaaat gccggcagcc cgcgccgccg acctcgcagc ccccgcgggc gcagccyttt 300
gcgcascgcc gggaccctgg cccctgtcga gtccagggcc aaggcttgtg ttcaatcgtg 360
tgaatggccg gcgggccccc tccacgtccc catccttcga ggggacccag gagacctaca 420
cagtggccca cgaggagaat gtccgctttg tgtccgaagc ctggcagcag gtgcaacagc 480
agctggatgg tggcccagcc ggtgagggcg ggccaaggcc tgtgcagtac gtggagagga 540
cccccaatcc ccggctgcag aactttgtgc ccattgacct agacgagtgg tgggcgcanc 600
agttcctggc gagaatcacc agctgttcct agtggctgct gggagggggc gctgctacac 660
ggccgacctg tcgccaggag agaagcatgg cgccctgccc acccactgcg cctggctggg 720
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gctgtcccaa ccaagctgcc atgccaaggg ccgaacccgt ctgacctcag ccctgctcac 840
tgtgcccagg gaccagcgna cacccctggg gctggcaggg aggagctcca ggctaataaa 900
gtggagaaac tgtcaaaaaa aaaaaaaaaa aanctcgagg gggggcccgn ncccaattnc 960

<210> 297
<211> 657
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (29)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (86)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (88)
<223> n equals a,t,g, or c

<400> 297
caaaagctgg agctccaccg cggtgacgnc cgctctagaa ctagtggatc cccgggctg 60
caggaattcg gcacgagctc gtgccngncc tttggagcag agaggaggca atggccacca 120
tggagaacaa ggtgatctgc gccctggtcc tggtgtccat gctggccctc ggcaccctgg 180
ccgaggccca gacagagacg tgtacagtgg ccccccgtga aagacagaat tgtggttttc 240
ctggtgtcac gccctcccag tgtgcaaata agggctgctg tttcgacgac accgttcgtg 300

gggtcccctg gtgcttctat cctaatacca tcgacgtccc tccagaagag gagtgtgaat 360
tttagacact tctgcaggga tctgcctgca tcctgacgcg gtgccgtccc cagcacggtg 420
attagtccca gagctcggct gccacctcca ccggacacct cagacacgct tctgcagctg 480
tgcctcggct cacaacacag attgactgct ctgactttga ctactcaaaa ttggcctaaa 540
aattaaaaga gatcgatatt aaaaaaaaaa gaaaaggaaa aaaaagggcg gccgtctaag 600
aggatccaag cttacgtaac gcgtgcatgc gaaggtcata gctcttctat agtgtca 657

<210> 298
<211> 892
<212> DNA
<213> Homo sapiens

<400> 298
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cctctgcctg cccctgtgga ctgatgctat cgcgcaccgt cccacgaccc caccccgagc 180
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cttagtctca atcccaggct cctcttgact ctgggcagct ttaatcaggt tgggcagcct 480
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cctggccctg cccagcctct gtcttgggag ctcagcccca gggttcggtc gtcagcagtt 720
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gcaccgctgt cagcctgagg aattaaagct ttggtgctgg gaaragcaaa aaaaaaaaaa 840
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaac tc 892

<210> 299
<211> 1624
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1621)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1623)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1624)
<223> n equals a,t,g, or c

<400> 299
cccgggctgc aggaattcgg cacgagagag gaggtcccac aggctcctgc cctggrctac 60

cgagtccccc gatggtgtta tacattaaat atccaggatg gagaagccac atgctactca 120
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<211> 1969
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (13)
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<210> 301
<211> 1882
<212> DNA
<213> Homo sapiens

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<220>
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<222> (223)
<223> n equals a,t,g, or c

<220>
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<222> (1840)
<223> n equals a,t,g, or c

<220>
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<222> (1849)
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ggaataaaaa taacaaaaaa at 1882

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<211> 2804
<212> DNA
<213> Homo sapiens

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<211> 3859
<212> DNA
<213> Homo sapiens

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<222> (581)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (889)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (890)

<223> n equals a,t,g, or c

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<211> 3378
<212> DNA
<213> Homo sapiens

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<222> (29)
<223> n equals a,t,g, or c

<220>
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<222> (3365)
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<213> Homo sapiens

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<222> (2166)
<223> n equals a,t,g, or c

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<221> misc feature
<222> (2168)
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<400> 308
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<211> 6163
<212> DNA
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<210> 310
<211> 2086
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1763)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1769)
<223> n equals a,t,g, or c

<400> 310
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cgcctcccca cgccgtcaga gatcctcagc aacgcgggtc tcaggtttga ggtggtcccc 180
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aagaaagcaa aagccaaaaa aaaaaaaaaa aaaaatttgg gggggg 2086

<210> 311
<211> 2163
<212> DNA
<213> Homo sapiens

<400> 311
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tccagcccta cctggcgcgg cggcccaagc tgcagctgag cgtgtacacc acgacgaggt 180
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aaa 2163

<210> 312
<211> 1397
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1397)
<223> n equals a,t,g, or c

<400> 312
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aaaaaaaaaa aaaaaan 1397

<210> 313
<211> 4106
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (344)
<223> n equals a,t,g, or c

<400> 313
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<210> 314
<211> 532
<212> DNA
<213> Homo sapiens

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<221> misc feature
<222> (497)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (498)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (502)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (524)
<223> n equals a,t,g, or c

<400> 314
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ttggaaaaaa aaaaaanngg gnggcgtttt aaagattcct cgangggggcc aa 532

<210> 315
<211> 1938
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1270)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1455)
<223> n equals a,t,g, or c

<400> 315
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agggctcagc aggcattttc ggaaagcagg gtgaaattgt ctcttcccag gaaaaagatt 1860
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cgcgatctag aactagtc 1938

<210> 316
<211> 818
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (55)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (814)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (818)
<223> n equals a,t,g, or c

<400> 316
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cccagcaact caaattcacc acctcggact cctgcgaccg catcaaagac gaatttcagc 180
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ccatagtatt atgktggccc gggggggggc ccanccan 818

<210> 317
<211> 837
<212> DNA
<213> Homo sapiens

<400> 317
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cgtgtgcgtg gacctgggtg actgggaggc caccgagcgg gcgctgggca gcgtgggccc 240
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gaacgccatc ctctttctgc tgagtgaccg aagtggcatg accacgggtt ccactttgcc 720
ggtggaaggg ggcttctggg cctgctgagc tccctccaca cacctcaagc cccatgccgt 780
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<210> 318
<211> 1448
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (878)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1198)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1395)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (1397)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1445)
<223> n equals a,t,g, or c

<400> 318
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ctgcaggcag gttgttgggt ttcgaggcca acggggccaa cgggtctaaa gcaggtaggg 180
gcggctgtga agtgaggggg tctaggggag aaaaggggac ggagagcaga ggaagggtgg 240
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cctgaggcgg aaccagtgct tggtggcaac gtgttcatgt ctgaagcagc ataacaaaga 360
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ggatgggagc atgagggcac cagtcacctt twaacctatt gggggacatt agcagtcaca 480
tgttgagtgc aaacgaggta cttttgtgca tgtktacaaa caggcagtta caagcgtgtc 540
attttcagtg gctccatttt aaatcagtct gctgcctcag aatcccgtac gcctgaaggt 600
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aagataaaca gagggagtag tgagaggctt ttccagtggg gaaaatgcct ctgtgggtca 1380
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aaacntgg 1448

<210> 319
<211> 1493
<212> DNA
<213> Homo sapiens

<400> 319
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taacttctcg ctgactgctt cacctcttac aagtctgccc atcccggaag taatgatgac 120
aaaatactcc aaccttttct tggaaagtca taacatctca ctgactgaac attccagtgt 180
gccagtggaa aaaaatatca ctttagaacg accttctgct gtagaactca catgtcagtt 240
cacaacttct ggggatgtga attcagtaaa tgtgacttgg aaaaaagggg atgaacaact 300
taagaattac catgtcagtg ccacagaagg catcctgtat acccagtaca agttttccat 360
cattaatagc gaacaactgg gaagctattc ttgtttcttt gaagaggaaa aggaacgaag 420
gggcacattt aatttcggag tccctgaagt tcagagaaaa aacaaaccat tgatcactta 480
tgtgggggat tccgttgtct tggtgtgtaa atgccgacac tgtgctcctt taaattggac 540
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tgcgatcaat ggaacaaacg cgaatgaaac aaggcttaag ataatgcagc tttcagaaga 660
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atatttgtaa taattttcat gtaatgktca ccctctgtca tattggataa aaacatcttt 1440
attaagaaat gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaagggcggc cgc 1493

<210> 320
<211> 609
<212> DNA
<213> Homo sapiens

<400> 320
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gagcatccag cgagtcctgc aggctgtgga taaagccaat ggatactgtt tcggagccca 180
agagcagcga acttggaagc catgatgtct gccgcaatgg gagccgactt ccatttctct 240
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ccagaaagtc gagcactggt cctagtcagg ctgtgatgaa atgtgctaca atacaagagt 600
ttattttct 609

<210> 321
<211> 502
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (458)
<223> n equals a,t,g, or c

<400> 321
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ctgaggtgaa ctgaagccag cagccccgca tcatgtcaaa gctcggccgg gccgcccggg 120
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ttttagtgaa gcctgacagg acatttgaaa ttaagattgg acagcccact gtttcctact 360

tcctgaaggc agcagctggg attgaaaagg gggcccggca aacagggaaa gaggtggcag 420
gcctggtgac cttgaagcat gtgtatgaga ttgcccgnat caaagctcag gatgaggcat 480
ttgcctgcag gatgtacccc tg 502

<210> 322
<211> 2630
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1952)
<223> n equals a,t,g, or c

<400> 322
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gcacctcccc tgccaactgc acctggctca tcctgggcag caaggaacag actgtcacca 360
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gctgtgtatc tgctgtccag cgctgtgatg gggttgatgc ctgtggcgat ggctctgatg 660
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<210> 323
<211> 1874
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (67)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1735)
<223> n equals a,t,g, or c

<400> 323
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tcgggangg cgggaggagg ggaacgccat atatagacct ggagagccgg gagcgcggag 120
agtggaatcg gtccgcggct cgagtgggtc tctagtccgg cgccagccgc ccggcccagc 180
cctcacaggt ccttcgtggt gcataccatc cgcctcccag ccatgcgctt cctcctgctt 240
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cacctcagcc ctaa 1874

<210> 324
<211> 2325
<212> DNA
<213> Homo sapiens

<400> 324
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tatgtttgac taaagctctc ttcatatgca ggtttataaa tttgttaggt ctgttgtccc 420
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aaaaa 785

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gacgacagaa gggtacggct gcgagaagac kacagaaggg tacggctgcg agaagackac 180
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acgn 244

<210> 327
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<212> DNA
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<400> 327

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tcccaccctc ccgcccccgcg gcagccctag ctccctccac ttggctcccc tggtcccgct 180
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gaactgaaga aagaagtttc tatggatgat cataaactta gccttgatga acttcatcgt 420
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aaagagaaac tttttcccag ctgggtgctg tggctcacac ctgtgaatcc cagccctttg 180
gnaggctgna gtgggcagat cgcttgagcc caggagtttg agatcagcct gggcaacatg 240
gtgaantcca tctctgtgaa aaatacaaaa attagccagg tgtggtggtg cgcgcctgtn 300
antcccagct actagggagg ctgaaggtgg gnggnttgnt tnagcccagg aggttgaggc 360
tgcattnggc tgggattcaa accatgttac tccntgacca ngtgngncct ntttcaaann 420
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ttagttgcac tagccatatt tcaaatactt gatggataca tgtggctagt ggctaacata 180
agggatagca cagatataaa acatttcctc ccaaagtgct gggattacag gcatgagcca 240
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gtaataggct gatatattac acttgttgat gtaanctgga tangtttctt tcttctccaa 360
ggacagcttt ttnaatattt aacantncca ttaatttttc agtttccggg agaattttat 420
aatttaaaat tgccgactta ngganaancc aattggncca accattacaa tanattttta 480
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ctggncagac accgntgnaa cgggnattat ttcaccctca gagagaggct gatcactatg 180
caaaaacaac tgggaggaaa cccagaagta tattgaatga gcagtgcaga ttagagttgc 240

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ccatatcgat gggcancaat tgncaattat tgtgnagcaa tacacacggg gtttccangg 300
gagtnttaaa tgccttaaag taattaaaan ccggggcaat nccnttttac ggatgttttg 360
ctggggtttc cgtttttaac caacattttt ntnggggncc gnccacaaat tttggggttg 420
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aatgtngcca ntgtctgtct gcagattggc tacccaactg ttgcatcagt accccattct 180
atcatcaacg ggtacnaacg antcctggcc ttgtctgtgg agacggatta caccttccca 240
cttgctgaan aagtcanggc ttcttggctg atccatctgc cttngtggct gctgcccngt 300
tggctgctgc caccacaact gctcctgctg ctgctgcncc ccancttaag ttnaaaccca 360
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ccatccggta cccctaccgt ccagatacca tcacccacgg gctcatggct ggggtcacca 180
tcacggccac cgtcatcctt gtctcggccg gggaagccta cctggtgtac acagaccggc 240
tctattctcg ctcggacttc aacaactacg tggctgctgt atacaaggtg ctggggactt 300
cctgtttggg gctgccgtga gccagtctct gacagacctg gccaagtaca tgattgggcg 360
tctgaagccc aattctaanc gtctgcgaac ccgattgaac cggtcaatgc tcgtnatgtg 420
cagtggagaa gtttgcaggg aacctnttga ttcacgagca gtgtttttaa tcggaatntc 480
tttgnn 486

<210> 333
<211> 268
<212> DNA

<213> Homo sapiens

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<220>
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<222> (264)
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ttcaactana agtatcanaa tatagcnttc cagaaaaccc cgaancanag tcactgacta 120
catcaaagtc tactacacct tgagaaaaca aatgaacgan aatctatttt cctcattcat 180
taccccaaca ataataggac tccctatcgt aattattntc actatgtttc caagcattga 240
tatncccatc acctaccccgn ctnntcaa 268

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<220>
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<220>
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<222> (447)
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<222> (463)
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cggaaaggag cgcctactaa ggacgccgtc gaggtccggg gcgcctcaac tctatagctc 60
taactggcta gaagtgccca acgtggaatg tttctttttt aaaggcggct cttgaagcga 120
cccggaagcg gaagtggaag aaagttctag tggcttgaga ttaagcctga tcaagatgac 180
aacctcccaa aagcaccgag acttcgtggc aganccoatg ggggagaacc agtggggaac 240
ctggctggga ttggtgaant cctgggcaag aaactggaag aaagggtttt gacaaggcta 300
tnttgtcttg gccatttctg gtgctaaaaa anataaaaac tctcccggaa tggtgaaaan 360
ctttttgggc cacccaacat cccgaatgtc cgatgctcca aaatgtgcan cctcttttat 420
gtctttggaa tctctncccc ccccccnatt tgaccaattg ganccccctt cctcaagaaa 480
atgttgttnc ccccanttcc ggttttgatt tccccac 517

<210> 335
<211> 297
<212> DNA
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<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

<220>
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<220>
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<222> (267)
<223> n equals a,t,g, or c

<220>
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<222> (286)
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<400> 335
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ggccgctcta gaactagtgg ggggcccggt acccaattcg ccctatagtg agtcgtatta 120
caattcactg gccgtcgttt tacaacgtcg tgacnnggaa aacntnnaat ncttccggct 180
cgtatgttgt gtggaattgt nagcggataa caattcacac aggnancagc tataaccatg 240
attnnnccaa gntcgaaatt aaccntnact aaaggggaca aaagtngggg ctccacg 297

<210> 336
<211> 386
<212> DNA
<213> Homo sapiens

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<220>
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<222> (128)
<223> n equals a,t,g, or c

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<222> (148)

<223> n equals a,t,g, or c

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<222> (187)
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<222> (200)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (204)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (244)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (251)
<223> n equals a,t,g, or c

<220>
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<222> (261)
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<220>
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<222> (265)
<223> n equals a,t,g, or c

<220>
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<222> (272)
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<220>
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<222> (275)
<223> n equals a,t,g, or c

<220>
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<220>
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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (380)
<223> n equals a,t,g, or c

<400> 336
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caaaatgctg ctgggtgttt atgcctactt tatagagcat aagcagcgca acacccttat 120
ctggttgncg acggatggtg atgcccgnga actttatgaa aaacccacgt tgagcccgac 180
tattngngat attccgtcgn tgcntggggc tggccccgtg gtatggcaaa aaagcaccgg 240
gttnaacaag ntcaaccatg naagngtttc anctnaatgg gggggncccc gtaacccaat 300
tngncctata agtnnatggg antttaanaa ttcaatnggc cctngntttt aaatggtgng 360
tgntnggcct tttttttttn gtttgt 386

<210> 337
<211> 506
<212> DNA
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<220>
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<222> (404)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (412)
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<220>
<221> misc feature
<222> (414)
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<220>
<221> misc feature
<222> (437)
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<220>
<221> misc feature
<222> (439)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (469)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (470)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (471)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (472)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (481)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (483)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (501)
<223> n equals a,t,g, or c

<400> 337
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caccactatg taccctggca ttgccgaccg aatgcagaag gagatcacgg ccctagcacc 120
cagcaccatg aagatcaaga tcattgcccc tccggaggcg caaatactct gtctggatcg 180
gtggctccat cctggcctct ctgtccacct tccagcagat gtggatcagc aaacagggaa 240
tacggtgaag ccgggccttc cattgtccac cgcaaatgct ttcttaaaac acttttcctg 300
gttcctnttc tgtcttttag gcacacaact gtggaatgtn cctgtgggaa tttatggccn 360
tttcagtttc tttttccaaa tcattcctag ggccaaagtt ttgnattggt tnanccatgg 420
ggttttttta aataaantnt ggaaataggg ttaattggtt aaaaaaaann nnaaaaaaaa 480
ntntgggggg gggggcccg ntaccc 506

<210> 338
<211> 623
<212> DNA
<213> Homo sapiens

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<222> (508)
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<220>
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<222> (509)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (513)
<223> n equals a,t,g, or c

<220>
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<222> (537)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (565)
<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

<220>
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<222> (612)
<223> n equals a,t,g, or c

<400> 338
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aagaaggagc tgtctgacat cgctcaccgc atcgtggcac ctggcaaggg catcctggct 120
gcagatgagt ccactgggag cattgccaag cggctgcagt ccattggcac cgagaacacc 180
gaggagaacc ggcgcttcta ccgccagctg ctgctgacag ctgacgaccg cgtgaacccc 240
tgcattgggg gtgtcatcct cttccatgag acactctacc agaaggcgga tgatgggcgt 300
cccttccccc aagttatcaa atccaagggc ggtgttgtgg gcatcaaggt agacaagggc 360
gtggtccccc tggcagggac aaatggcgag actaccaccc aagggttgga tgggctgtct 420
gagcgctgtg cccagtacaa ngaaggacgg agctgacttc ggccaagtgg cgttgtgtgc 480
ttaagaatgg gggaacacac cccctcannc ctnggcatca tggaaaatgc caattgntct 540
ggccccgtat gccagtatct ggcancagaa tgcattgggc cattcgggga gtctgananc 600
tcctgatggg ancatgactt gaa 623

<210> 339
<211> 344
<212> DNA
<213> Homo sapiens

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<222> (157)
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<221> misc feature
<222> (171)
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<222> (210)
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<222> (298)
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<222> (317)
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<220>
<221> misc feature
<222> (330)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (343)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (344)
<223> n equals a,t,g, or c

<400> 339
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tttttatat ttcaactaaa agtatcanaa tatagctttc cagaaaaccc cgaaccaaag 120
tcactgacta catcaaagtc tactacacct tggaganaac aaatgaacga naatctattt 180
tcctcattca ttaccccaac aataataggn ctccctatcg taattattat cactatgttt 240
ccaagcatta tattcccatc acctacccga ctaatcaata atcgactcat ctccattnca 300
acaatggatt agtgcantga acatgcaaan gcaaggatta tcnn 344

<210> 340
<211> 345
<212> DNA
<213> Homo sapiens

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<220>
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<222> (31)
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<220>
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<222> (172)
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<220>
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<222> (173)
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<220>
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<222> (296)
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<220>
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<222> (313)
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<221> misc feature
<222> (343)
<223> n equals a,t,g, or c

<220>
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<222> (345)
<223> n equals a,t,g, or c

<400> 340
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ggaattcccg ggtcgaccca cgcgtccngn aggaggggac agctgcgggc gcggggaggg 120
ggcgccgngc cgcgnggngc catggnggac agnagagccg ggagtccgag anncgggccc 180
gcagcccgag atgtcgccgc catggcttcg ccgcagctct gccgcgcgct ggtgtcggcg 240
caatgggtgg cggaagcgct gcgggccccg cgcgctgggg cagcctctgc agctgntagg 300
acgcctcctg gtnacctggc cggaagctgg ggggcgcgna cgncn 345

<210> 341
<211> 170
<212> DNA
<213> Homo sapiens

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<220>
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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (43)
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<221> misc feature
<222> (164)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (170)
<223> n equals a,t,g, or c

<400> 341
acccacgcgt ccgcccacgn tcncgactag ttctagatcg cgnacggccg ctctagagga 60
tccaagctta cttggacatg catgcnacgt catagctctt ctatagtgtc acctaaattc 120
aattcactgg ccgtcgtttt acaacgtcgt gactgggaan atnntaaaan 170

<210> 342
<211> 387
<212> DNA
<213> Homo sapiens

<220>
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<222> (238)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (273)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (328)
<223> n equals a,t,g, or c

<220>
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<222> (351)
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<220>
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<222> (366)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (384)
<223> n equals a,t,g, or c

<400> 342
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agagaattat gcagtgctgc cataaccatg agtgataaca ctgcggccaa cttacttctg 120
acaacgatcg gaggaccgaa ggagctaacc gctttttgc acaacatggg ggatcatgta 180
actcgccttg atcgttggga accggagctg aatgaagcca taccaaacga cgagcgtnac 240
accacgatgc ctgtagcaat ggcaacaacg ttngcaaact attaactggc ggactactta 300
ctctagcttc ccggcaacaa tttatagnct tggtggnggc gggtaaagtt ncaaggccca 360
tttttnggtt tggccttccg gttngtt 387

<210> 343
<211> 186
<212> DNA
<213> Homo sapiens

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<222> (64)
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<221> misc feature
<222> (71)
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<222> (109)
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<220>
<221> misc feature
<222> (152)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (153)
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<220>
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<222> (160)
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<220>
<221> misc feature
<222> (183)
<223> n equals a,t,g, or c

<400> 343
gctgcaggaa attaacagag tctacnagga aatgtacaag actgatctgg agaaagacat 60
tatntcggac ncatctggtg acttccgcaa gctgatggtt gccctggcna aaggttaaaa 120
aacagaagaa tggtccgtcc ttgaatatga anngaatgan ccacatgccc ggatttcctt 180
ganccc 186

<210> 344
<211> 611
<212> DNA
<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (285)
<223> n equals a,t,g, or c

<400> 344
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cgctctagaa ctagtggatc ccccgggctg caggaattcg gcacgagctg cgttgggctc 120
cgggaagccg ttcgggctgg ggctgtcggc cgcggggcgg aggcactcgc gcgggggatg 180
gcccactgcg tgaccttggt tcagctgtcc atttcctgtg accatctcat tgacaaggac 240
atcggctcca agtctgaccc actctgcgtc cttttacagg atgtnggagg gggcagctgg 300
gctgagcttg gccggactga acgggtgcgg aactgctcaa gccctgagtt ctccaagact 360
ctacagcttg agtaccgctt tgagacagtc cagaagctac gctttggaat ctatgacata 420
gacaacaaga cgccagagct gagggatgat gacttcctag ggggtgctga gtgttcccta 480
ggacagattg tgtccagcca ggtactgact ctccccttga tgctgaagct ggaaaacctg 540
ctgggcgggg gaccatcacg gtctcagctc aggaattaaa ggacaatcgt gtagtaacca 600
tggaggtaga g 611

<210> 345
<211> 344
<212> DNA
<213> Homo sapiens

<220>
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<222> (296)
<223> n equals a,t,g, or c

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<222> (329)
<223> n equals a,t,g, or c

<220>
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<222> (331)
<223> n equals a,t,g, or c

<220>
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<223> n equals a,t,g, or c

<400> 345
tttccttcta cagtattcct gaatttgacg aatggaaaaa acatatagaa aaccagaaag 60
cctggaaaat aaagtactat aaaggattgg gtactagtac agctaaagaa gcaaaggaat 120
attttgctga tatggaaagg catcgcatct tgtttagata tgctggtcct gaagatgatg 180

ctgccattac cttggcattt agtaagaaga agattgatga cagaaaagaa tggttaacaa 240
attttatgga agaccggaga cagcgtagct acatggctta ccagaggant gattcnctct 300
caactcagac atgaaagatc tataccacnc ntgttgatgg cntt 344

<210> 346
<211> 506
<212> DNA
<213> Homo sapiens

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<222> (392)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (452)
<223> n equals a,t,g, or c

<220>
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<222> (453)
<223> n equals a,t,g, or c

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<222> (480)
<223> n equals a,t,g, or c

<220>
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<222> (495)
<223> n equals a,t,g, or c

<400> 346
ggaaaagccc aaggaaaaag caaagaatag caaaaaaaag ggggccaaga aggaagtggt 60
tgggattggt cttctttttt cttcagtgag ttttttcccc aacaggttct gatggtcctt 120
tggctaccag caaaccagtc cctgcagaaa agtcaggtct tccagtgggt cctgagaacg 180
gagtagaact ttccaaagag gagctgatcc gcaggaagcg cgaggagttc attcagaagc 240
atgggagggg tatggagaag tccaacaagt ccacgaagtc agatgctcca aaggagaagg 300
gcaaaaaagc accccgggtg tgggaactgg gtggctgtgc taacaaagaa atgttggatt 360
acagtacttc caccaccaat ggaacccctg angcttgcct tgtctgagga cattaacctt 420
gattccaagg gactgggtct ggggggcact tnnggatctg gactgcacac tntgatgacn 480
aagggcttgt taaantttcc aaacta 506

<210> 347

<211> 444
<212> DNA
<213> Homo sapiens

<220>
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<222> (289)
<223> n equals a,t,g, or c

<400> 347
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gctacgattt cagagtaccc tggtaatagc tgagcatgca aatgattccc tagcacccat 120
tactttaaat accattactg cagccacacg ccttggaggt gaagtgtcct gcttagtagc 180
tggaaccaaa tgtgacaagg tggcacaaga tctctgtaaa gtagcaggca tagcaaaagt 240
tctggtggct cagcatgatg tgtacaaagg cctacttcca gaggaactna caccattgat 300
tttggcaact cagaagcagt tcaattacac acacatctgt gctggagcat ctgccttcgg 360
aaagaacctt ttgcccagag tagcagccaa acttgaggtt gccccgattt ctgacatcat 420
tgcaatcaag tcacctgaca catt 444

<210> 348
<211> 358
<212> DNA
<213> Homo sapiens

<220>
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<223> n equals a,t,g, or c

<220>
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<222> (52)
<223> n equals a,t,g, or c

<220>
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<222> (187)
<223> n equals a,t,g, or c

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<222> (280)
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<220>
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<222> (295)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (301)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (317)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (348)
<223> n equals a,t,g, or c

<400> 348
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gacagacatg gaatcccaac cgcacaatgg gaaggctttc accaaacctg aaaggaagcc 120
tgcagcttca ttttgagtgc agacttccct gctttggttg tgaaaggcca gtggtcttgc 180
agctggnaaa aggggtgatt gttgcaaaga gcaaagaaga ggcctgcaag ctgtacaaga 240
gatcatgcag gtaggctggg tcttctggaa aaatttactn ttgtattcat actgnatgaa 300
ntaccgtttt aagtttnaaa aatgttcctc acattaaggg aaattctntt ttgcaacc 358

<210> 349
<211> 321
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (187)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (206)
<223> n equals a,t,g, or c

<220>
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<222> (240)
<223> n equals a,t,g, or c

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<222> (294)
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<220>
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<222> (295)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (301)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (316)
<223> n equals a,t,g, or c

<400> 349
ggcgctttgc tctgtccacc aagattcctg acaccaaagg ctgcttgcag tgtcgtgtgg 60
tgcggaaccc ctacacgggt gccaccttcc tgctggccgc cctgcccacc agcctgctcc 120
tgctgcagtg gtatgagccg ctgcagaagt ttctgctgct gaagaacttc tccagccctc 180
tgcccanccc agctgggatg ctgganccgc tggtgctgga tgggaaggag ctgccgcagn 240
gtttttttgg ggccgaaggg cctaaagggc ccggttgccg gttcctgttc caannсctgc 300
ncctgggagg ttggcnttaa g 321

<210> 350
<211> 742
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (618)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (653)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (658)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (683)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (689)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (702)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (707)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (714)
<223> n equals a,t,g, or c

<220>
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<222> (719)
<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

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<222> (734)
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<400> 350
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cttcaatgca gaagtgcttt tccgagaaga ctgctccccg gacgagttca tcgatgtgat 120
cgtgggcaac cgggtgtaca tgccctgcct gtatgtttat aacaaaatcg accagatctc 180
catggaagag gtggaccgcc tggcccgaaa acccaacagt gtggtcatca gctgcggcat 240
gaagctgaac ctggactatc tgctggagat gctctgggag tacttggccc tgacctgcat 300
ctacaccaag aagagaggac agaggccaga cttcacagac gccatcattc tccggaaagg 360
ggcctcagtg gagcacgtgg gcaccagcac caagtacagt ccgcagcggg tgggcctgac 420
ccacaccatg gagcatgagg acgtcatcca gatcgtgaag aagtaacggc gcctgccggg 480
ccttccgccc acctgctcgt ctcccttggg aggtggtccc actgggacac acaaacaccc 540
aaacagaaaa atacaaatac acgtacccca agaaggggtc cctcaagtct ctgctattta 600
cagaagtttc ttcagtangc agaccaaaaa tgtgttgggc aaaagggctc ggntggangc 660
atttccata agactgagcc ctnttcatng gggggttttga gnttgantgc ttancctgna 720
tntgtgcctc caanccccctg ac 742

<210> 351
<211> 272
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (167)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (251)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (272)
<223> n equals a,t,g, or c

<400> 351
aatcaggcgg gactgacggc agatcgtatg ctggtcctgt ccagagccgg gcaggcggca 60
gggctgacgt ttaaccagac cagcgagtca ctcagcgcac tggttaaggc gggggtaagc 120
ggtgaggctc agattgcgtc catcagccag agtgtggcgc gtttctnctc tgcatccggc 180
gtggaggtgg acaaggtcgt tgaagccttc gagggggccc cgtacccatt tgcctatagt 240
aagcgtatta naataattgc cgtgttttaa an 272

<210> 352
<211> 256
<212> DNA
<213> Homo sapiens

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<222> (170)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (236)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (248)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (251)
<223> n equals a,t,g, or c

<220>
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<222> (252)
<223> n equals a,t,g, or c

<400> 352
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gcggggcccc agctgggacc ccttccgcga ctggtacccg catagccgcc tcttcgacca 120

ggccttcggg ctgccccggc tgccggagga gtggtcgcag tggttaggcn gcagcagctg 180
gccaggctac gtgcgccccc tgccccccgc cgcatcgaga gccccgcagt ggccgngccc 240
gctacagncg nncgct 256

<210> 353
<211> 592
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (35)
<223> n equals a,t,g, or c

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<221> misc feature
<222> (54)
<223> n equals a,t,g, or c

<220>
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<222> (93)
<223> n equals a,t,g, or c

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<222> (277)
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<220>
<221> misc feature
<222> (485)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (522)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (545)
<223> n equals a,t,g, or c

<400> 353
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gctcactcgt tgggtccgtg ccacctttaa aanctgtaac actcaccgcg aaggtctgca 120
acttcactcc tggggccagc aagaccacga gtgcaccgag aggaatgaac aactctggac 180
acaccatctt taagaaccgt aatactcacc gcaagggtct gcaacttcat tcttgaagtc 240
agtgaggcca agaacccatc aattccgtac acatttnggt gactttgaag agactgtcac 300
ctatcaccaa gtggtgagac tattgccaag cagtgagact attgccaagt ggtgagacca 360
tcaccaagcg gtgagactat cacctatcgc caagtggtcc taagtgtgaa cgtgaagtcc 420
ccagccctgc tgctgagcca gttgctgccc tacatggaga acaagaaggg tgctgtcatn 480
ctggnctctt ccattgcagc ttataatcca gtagtggcgc tnggtgtcta caatgtcagc 540
aaganagagc tgctggggtc tcactagaac actggcattg ggcttggccc cc 592

<210> 354
<211> 539
<212> DNA
<213> Homo sapiens

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<222> (4)
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<220>
<221> misc feature
<222> (223)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (225)
<223> n equals a,t,g, or c

<400> 354
cacnaaccct cactaaaggg aacaaaagct ggagctccac cgcggtgacg gccgctctag 60
aactagtgga tcccccgggc tgcaggaatt cggcacgagt cgtctcaggc tcgtagttcg 120
ccttcaacat gccggaacca gcgaagtccg ctcccgcgcc caagaagggc tcgaagaaag 180
ccgtgactaa ggcgcagaag aaggacggca agaagcgcaa ggnanccgca aggagagcta 240
ctccgtatac gtgtacaagg tgctgaagca ggtccacccc gacaccggca tctcctctaa 300
ggccatggga atcatgaact ccttcgtcaa cgacatcttc gaacgcatcg cgggtgaggc 360
ttcccgcctg gcgcattaca acaagcgctc gaccatcacc tccagggaga tccagacggc 420
cgtgcgcctg ctgctgcccg gggagttggc caagcacgcc gtgtccgagg gcaccaaggc 480
cgtcaccaag tacaccagcg ctaagtaaac ttgccaagga gggactttct ctggaattt 539

<210> 355
<211> 435
<212> DNA
<213> Homo sapiens

<220>
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<222> (296)
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<220>
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<222> (299)
<223> n equals a,t,g, or c

<220>
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<222> (396)
<223> n equals a,t,g, or c

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<222> (421)
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<220>
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<222> (422)
<223> n equals a,t,g, or c

<220>
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<222> (424)
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<400> 355
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atgaggacac actctctgtg gcactgccat atttctggga gcactttgat aaggacggct 120
ggtccctgtg gtactcagag tatcgcttcc ctgaagaact cactcagacc ttcatgagct 180
gcaatctcat cactggaatg ttccagcgac tggacaagct gaggaagaat gccttcgcca 240
gtgtcatcct ttttggaacc aacaatagca gctccatttc tggagtctgg gtcttnccng 300
gccaggagct tgcctttccg ctgagtccag attggcaagt ggactacgaa gtcatacaca 360
tggcggaaac tggatctggc aagcgaggag acccanacgc tggttcgaga gtacttttnc 420
nngngagggg gcctt 435

<210> 356
<211> 502
<212> DNA
<213> Homo sapiens

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<222> (317)
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<220>
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<222> (324)
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<220>
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<222> (497)
<223> n equals a,t,g, or c

<220>
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<222> (499)
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<400> 356
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gaagaatgaa cagaagggag agaagattcc tcggtgcttg ccagtttgtg ggaagcccgt 120
gaaccccgtg gaacagaggc agcgcatcat cggagggcaa aaagccangg ggatagtggg 180
ggcgttttg cagtaaggga cccgaacact gatcgctggg tggccacggg catcgtgtnc 240
ctngggcatc gngtgcagca gggccttatg gcttnttaca ccaaagtnct cnaacttncg 300
tggccttgga tcaagnnaga cctngganca ggaggactnc cgccccanca ttcactaggt 360
tccnaatcca gngagcagtt tcgcanaaan canccanaca canctteccc ctntttngnn 420
acccnncagn gtctctnttn anatncctnc tngcacnnna ncccacaacc cccccncncc 480
ccccnccccc ccccccncnc cc 502

<210> 357
<211> 440
<212> DNA
<213> Homo sapiens

<220>
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<222> (262)
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<220>
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<222> (293)
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<220>
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<222> (300)
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<220>
<221> misc feature
<222> (316)
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<220>
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<222> (339)
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<221> misc feature
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<220>
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<221> misc feature
<222> (418)
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<221> misc feature
<222> (426)
<223> n equals a,t,g, or c

<400> 357
aatatatcga acagtcaggt taacaggctg cggcattttg tccgngccgg gcttcgctca 60
ctgttcaggc cggagccaca gaccgccgtt gaatgggcgg atgctaatta ctatctcccg 120
aaagaatccg cataccagga agggcgctgg gaaacactgc cctttcagcg ggccatcatg 180
aatgcgaatg ggcagcgact acatccgtga gtggaatgtg gtgaagtttg cccgtntcgg 240
ttattccaaa atgctgctgg gngtttatgc ctactttata gggcataagc agnggaacan 300
ccttatttgg tttccncagg atggtggatg cccgagaant ttttggaaaa cccacgttgn 360
gncgattatt tcgggganat ttccggngnt gttggggttt gnccccntgg gttttggnaa 420
aaaganccgg gtaaaaggtt 440

<210> 358
<211> 234
<212> DNA
<213> Homo sapiens

<220>
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<222> (16)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (46)
<223> n equals a,t,g, or c

<220>
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<222> (92)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (162)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (166)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (175)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (208)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (230)
<223> n equals a,t,g, or c

<400> 358
ggaaagggtg tttatncctc atggactaat tatggacagg actgancgtt ttgctcgaaa 60
tgtgatgaag gagatgggag gccatcacat tntagtcctc tttttgctca agggggggcta 120
taaatttttt gctgacctgc tggattacat caaaggactg antagnaaat agtgnataga 180
tccattcctc atgaactgtg gatttttngc agatctgaag agctattgtn atga 234

<210> 359
<211> 668
<212> DNA
<213> Homo sapiens

<220>
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<222> (15)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (19)
<223> n equals a,t,g, or c

<220>
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<222> (20)
<223> n equals a,t,g, or c

<220>
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<222> (295)
<223> n equals a,t,g, or c

<220>
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<222> (512)
<223> n equals a,t,g, or c

<220>
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<222> (552)
<223> n equals a,t,g, or c

<220>
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<222> (558)
<223> n equals a,t,g, or c

<220>
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<222> (559)
<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

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<220>
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<222> (593)
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<220>
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<222> (659)
<223> n equals a,t,g, or c

<220>
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<222> (667)
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<400> 359
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aagctggtac gcctgcaggt accggtccgg aattcccggg tcgacccacg cgtccggggt 120
gtttgaggta cataagaaaa atgtaagggg tgaattcact tattatgaaa tacaagataa 180
tacagggaag atggaagtgg tggtgcatgg acgactgacc acaatcaact gtgaggaagg 240
agataaactg aaactcacct gctttgaatt ggcaccgaaa agtgggaata ccggngagtt 300
gagatctgta attcatagtc acatcaaggt catcaagacc aggaaaaaca agaaagacat 360
actcaatcct gattcaagta tggaaacttc accagacttt ttcttctaaa atctggatgt 420
cattgacgat aatgtttatg gagataaggt ctaagtgcct aaaaaaatgt acatatacct 480
ggttgaaata caacactata catacacacc ancatatata ctagcttgtt aatcctatgg 540
aaatggggta tntggagnnc ttttttaatt tttcatagnt tttttttnat aanaatggca 600
tattttggat ctacaacttc tatgatttga aaaaatacct taacccttat cttttttgng 660
aaaaaana 668

<210> 360
<211> 401
<212> DNA
<213> Homo sapiens

<400> 360
caccattacc agcggcggca atcctccggc cttttccctg acaccggacg gaaagctgac 60
cgctaaaaat gcggatatca gtggcagtgt gaatgcgaac tccgggacgc tcagtaatgt 120
gacgatagct gaaaactgta cgataaacgg tacgctgagg gcggaaaaaa tcgtcgggga 180
cattgtaaag gcggcgagcg cggcttttcc gcgccaggtg gaaagcagtg tggactggcc 240
gtcaggtacc cgtactgtca ccgtgaccga tgaccatcct tttgatcgcc agatagtggt 300
gcttccgctg acgtttcgcg gaagtaagcg tactgtcagc ggcaggacaa cgtattcgat 360
gtgttatctg aaagtactga tgaacggtgc ggtgatttat g 401

<210> 361
<211> 273
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (156)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (189)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (236)
<223> n equals a,t,g, or c

<400> 361
acccgaacac ggcactggtc ggcgtgcagg tggactcgga gcagttcggc agccagcagg 60
tgagccgtaa ttatcatctg cgcgggcgta ttctgcaggt gccgtcgaac tataacccgc 120
agacgcggca atacagcggt atctgggacg gaacgnttaa accggcatac agcaacaaca 180
tggcctggng tctgtgggat atgctgaccc atccgcgcta cggcatgggg aaacgncttg 240
gtgcggcgga tgtggataaa tgggcgctgt atg 273

<210> 362
<211> 248
<212> DNA
<213> Homo sapiens

<220>
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<222> (5)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (37)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (41)
<223> n equals a,t,g, or c

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<222> (52)
<223> n equals a,t,g, or c

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<222> (74)
<223> n equals a,t,g, or c

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<222> (145)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (161)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (185)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (194)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (210)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (218)
<223> n equals a,t,g, or c

<400> 362
cgtcngtcgg gcgagcgatg atgcggaagg ttacctngat nttttcaaag gnaagataac 60
cgaatcccat ctcngcaagg agctgctgga aaaagtcgag ctgacggagg ataacgccag 120
cagactggag gagttttcga aagantggaa ggatgccagt nataagtgga atgccatgtg 180
ggctntcaaa attnagcaga ccaaagacgn caaacgantt ttattctgct atttagtagt 240

aagatcag 248

<210> 363
<211> 149
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (131)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (137)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (144)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (145)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (147)
<223> n equals a,t,g, or c

<400> 363
tgccggactt tcatcgtgag gatgactggt ggcgtaacgg ccagaatctc tatctggata 60
atctggaggc gacggggctg tatcaggtgc cgttgtcagc ggcacagccg ggcgatgtgc 120
tgctgtgctg ntttggntca tcanngncg 149

<210> 364
<211> 352
<212> DNA
<213> Homo sapiens

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<223> n equals a,t,g, or c

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<221> misc feature
<222> (93)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (196)
<223> n equals a,t,g, or c

<220>
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<222> (319)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (322)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (325)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (338)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (340)
<223> n equals a,t,g, or c

<400> 364
gcanaaagaa aatggcacag taacagctgc caatgccagt acactgaatg atggagcagc 60
tgctctggtt ctcatgacgg cagatgcagc gangaggctc aatgttacac cactggcaag 120
aatagtagca tttgctgacg ctgctgtaga acctattgat tttccaattg ctcctgtata 180
tgctgcatct atggtnctta aagatgtggg attgaaaaaa gaagatattg caatgtggga 240
agtaaatgga agcctttagt ctggttgtac tagcaaacat taaaaatgtt ggagattgga 300
tccccaaaaa gtgaatatnc anggnaggag ctgtttcncn ggggacatcc ca 352

<210> 365
<211> 272
<212> DNA
<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>
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<222> (42)
<223> n equals a,t,g, or c

<220>
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<222> (44)
<223> n equals a,t,g, or c

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<222> (47)
<223> n equals a,t,g, or c

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<222> (80)
<223> n equals a,t,g, or c

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<222> (91)
<223> n equals a,t,g, or c

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<221> misc feature
<222> (116)
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<220>
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<222> (145)
<223> n equals a,t,g, or c

<220>
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<222> (190)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (226)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (242)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (260)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (261)
<223> n equals a,t,g, or c

<400> 365
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ggcttgtgcc gctgctggan tgacagcctt ncgaggcttt gctgtctcgg cacggnaggt 120
ctggcaaacc anggacagac caggnacatg ggaccaaagc cggaacctcc tgctcaacgg 180
gaagtcctan cccaccaaag tgcgcctgat ctggggggc tccctncccc cagtcaagcg 240
gncggcggat gaactggatn nacgccccgg at 272

<210> 366
<211> 254
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (23)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (192)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (208)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (209)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (236)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (244)
<223> n equals a,t,g, or c

<400> 366
ggctctacta ggactcacta tanggaaagc tggtacgcct gcaggtaccg gtccggaatt 60
cccgggtcga cccacgcgtc cgcttctctg cctagaaggg ataatattat cactcttcgt 120
tataataaca atcaccatct taattaacca ccttacatta gccagcataa cccctatcat 180
ccttcttgta tntgcagcct gtgaagcnnc actggggctt atccctttta gttatnatct 240
caantacata cgga 254

<210> 367
<211> 185
<212> DNA
<213> Homo sapiens

<400> 367
gattggattc gacaacaaaa aagacctgct tatctcggtg ggcgatttgg ttgatcgtgg 60
tgcagagaac gttgaatgcc tggaattaat cacattcccc tggttcagag ctgtacgtgg 120
aaaccatgag caaatgatga ttgatggctt atcagagcgt ggaaacgtta atcactggct 180
gctta 185

<210> 368
<211> 458
<212> DNA
<213> Homo sapiens

<220>
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<220>
<221> misc feature
<222> (4)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
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<222> (15)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (27)
<223> n equals a,t,g, or c

<220>
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<222> (170)
<223> n equals a,t,g, or c

<220>
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<222> (193)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (232)
<223> n equals a,t,g, or c

<220>
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<222> (246)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (250)
<223> n equals a,t,g, or c

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<221> misc feature
<222> (316)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (340)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (395)
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<220>
<221> misc feature
<222> (399)
<223> n equals a,t,g, or c

<220>
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<222> (404)
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<220>

<221> misc feature
<222> (415)
<223> n equals a,t,g, or c

<220>
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<222> (433)
<223> n equals a,t,g, or c

<400> 368
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ccggagtgag ccttgaacgc ctggacctgg acctcacagc tgacagccag ccacccgtct 120
tcaaggtctt cccaggcagt accactgagg actacaacct tattgttatn gaacgtggcg 180
ctgccgctgc acnaccggcc agccagggac tgcgcctgca ggaacccctg gngccccacc 240
cctggntggn atggccattg tcaaggagga ggagacggag gctgccattg gagcccctcc 300
tactgccact gagggncctg agaccaaacc tgtgcttatn gctcttgagg agggtcctgg 360
tgctgagggt tcccggctgg actcactagt ggcanaacna ctcnggctgg aagtngtagc 420
tctgagggac tcngccccag tgttggccgg gacctgat 458

<210> 369
<211> 288
<212> DNA
<213> Homo sapiens

<220>
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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (17)
<223> n equals a,t,g, or c

<220>
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<222> (47)
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<222> (71)
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<222> (103)
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<222> (114)
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<220>
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<222> (239)
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<400> 369
gcgctggagc tgctngngca ctgcggcgtg tgcagagagc gcctgcnacc cgaganggag 60
ccccgcctgc ngccctgttt gcactcggcc tgtagtgcct gcntagggcc cgcngccccg 120
ccgccgccaa cagctcgggg gacggcgggg cggcgggcga cggcaccgtg gtggactgtc 180
ccgtgtgcaa gcaacagtgc ttctccaaag acatcgtgga gaatnatttc atgcgtgana 240
gtggcagcaa ggctgccacc gacgcccagg atgcgaacca gtgctgca 288

<210> 370
<211> 292
<212> DNA
<213> Homo sapiens

<220>
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<220>
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<222> (53)
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<222> (141)
<223> n equals a,t,g, or c

<220>
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<222> (263)
<223> n equals a,t,g, or c

<400> 370
ccatctttgc attgttcctc atccgcctcc ttgctcgccg cagccgnctc cgncgcgcgn 60
ntcctccgcc gccgcggact ccggcagctt tatcgccaga ntccctgaac tctcgctttc 120
tttttaatcc cctgcatcgg ntcaccggcg tgccccacca tgtcagacgc agccgtagac 180
accagctccg aaatcaccac caaggactta aaggagaaga aggaagtttt ggaaagaggc 240
agaaaatgga agagacggcc ctncttaacg gggaatgcta atttagggaa at 292

<210> 371
<211> 477
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (35)
<223> n equals a,t,g, or c

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<221> misc feature
<222> (276)
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<220>
<221> misc feature
<222> (313)
<223> n equals a,t,g, or c

<220>
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<222> (342)
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<220>
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<222> (410)
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<220>
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<222> (427)
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<220>
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<222> (434)
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<220>
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<222> (447)
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<220>
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<223> n equals a,t,g, or c

<220>
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<222> (451)
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<400> 371
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tggttccaag cataaaagaa cggacagatc aattttatgt tgtttacgaa aaggagaatc 120
tggccagtca tggcaagggt taacaaaaga aagggcaaag cttaattggc ttagtgtcga 180
cttcaataat tgggaaagac tgggaagatg attcaaatga agacatgtct aattttgaat 240
cgtttctctg aggattcaca agacagtgat gatggnaaaa atgccagatc tgggagtaag 300
ggaatattgt ccntcacctg ggtttttgag gaaaggaaaa tnaactttct ctggcaaggt 360
tttccataat ttgngaggaa ttccccgagt ttgttagcnc ctaaagggcn gttatgctcg 420
tatttgnccc actntaaccc ctttttnnca nccggtttgt ttttttaaaa gggcttc 477

<210> 372
<211> 443
<212> DNA
<213> Homo sapiens

<220>

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<220>
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<222> (74)
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<220>
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<222> (123)
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<220>
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<222> (293)
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<220>
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<222> (430)
<223> n equals a,t,g, or c

<400> 372
ggcagagcac tgtnaaacta gaacatgcta aatctgttgc ttccagagcc actgtcctcc 60
agaaganatc cttnacccct gtaggaatgt ttttgaaact aaatttnatg aacgtnaaat 120
ttnccagtgg ttattatgaa cttccttgtc gaagttgaaa ggtgaacaac nctnatattg 180
caaataccgt agagcttcag agtgcaagat tctccactgn angttgggca ttcacaaatg 240
ttggatcttt cccaccgtgg gatgaagggt tcagaggcat tgcacccaaa atnacccggg 300
tgaacatacc cagnccaaag cccaggggna cattnatcgn ggacaggccc nccagaattt 360
ggcntgttct ttnccagttg gtaggtgtgg aacttggggt tgaattnatt ncttaaccga 420
attttnccgn ttccttaacc gag 443

<210> 373
<211> 464
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (20)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (235)
<223> n equals a,t,g, or c

<400> 373
cggatccgca ggcgcacgtn gcgatgttgt cctctacagc catgtattcg gctcctggca 60
gagacttggg gatggaaccg cacagagccg cgggcccttt gcagctgcga ttttcgccct 120
acgttttcaa cggaggtact atactggcaa ttgctggaga agattttgca attgttgctt 180
ctgatactcg attgagtgaa gggttttcaa ttcatacgcg ggatagcccc aaatnttaca 240
aattaacaga caaaacagtc attggatgca gcggttttca tggagactgt cttacgctga 300
caaagattat tgaagcaaga ctaaagatgt ataagcattc caataataag gccatgacta 360
cgggggcaat tgctgcaatg ctgtctacaa tcctgtattc aaggcgcttc tttccatact 420
atgtttacaa catcatcggt ggacttgatg aagaaggaaa gggg 464

<210> 374
<211> 369
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (216)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (218)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (219)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (221)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (332)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (357)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (360)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (363)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (369)
<223> n equals a,t,g, or c

<400> 374
ggcacagcct ctacagccat gtattcggct cctggcagag acttggggat ggaaccgcac 60
agagccgcgg gccctttgca gctgcgattt tcgccctacg ttttcaacgg aggtactata 120
ctggcaattg ctggagaaga ttttgcaatt gttgcttctg atactcgatt gagtgaaggg 180
ttttcaattc atacgcggga tagccccaaa tgttgncnna ntaacagaca aaacagtcat 240
tggatgcagc ggttttcatg gagactgtct tacgctgaca aagattattg aagcaagact 300
aaagatgtat aagcattcca ataataaggc cntgactacg gggggcaatg ctggcangcn 360
gtnctacan 369

<210> 375

<211> 313
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (32)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (249)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (259)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (268)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (293)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (308)
<223> n equals a,t,g, or c

<400> 375
taccettcat cactaaaggc cgcctgtgcg tnttttttta cgggattttt ttatgtcgat 60
gtacacaacc gcccaactgc tggcggcaaa tgagcagaaa tttaagtttg atccgctgtt 120
tctgcgtctc tttttccgtg agagctatcc cttcaccacg gaggaaagtc tatctctcac 180
aaattccggg actggtaaac atggcgctgt acgtttcgcc gattgtttcc ggtgaaggtt 240
atcccgttnc cctggcggnt tccacctntg aatttaaggc cgggataatg tcnaagcccg 300
aagcatgnaa gtg 313

<210> 376
<211> 375
<212> DNA
<213> Homo sapiens

<400> 376
cgggttccgg tgaccacgaa ggcggcaaag gcgacggaat ggaggaggtg cctcacgact 60
gtccaggggc cgacagcgcc caggcgggca gaggggcttc atgtcaggga tgccccaacc 120
agcggctgtg cgcttctgga gcgggggcca ctccggacac ggctatagag gaaatcaaag 180

agaaaatgaa gactgtaaaa cacaaaatct tggtattgtc tgggaaaggc ggtgttggga 240
aaagcacatt cagcgcccac cttgcccatg gcctagcaga ggatgaaaac acacagattg 300
ctcttctaga catcgatata tgtgggccat cgattcccaa gataatggga ttggaaggag 360
agcaggttca ccaga 375

<210> 377
<211> 434
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (17)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (22)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (32)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (33)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (47)
<223> n equals a,t,g, or c

<220>
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<222> (58)
<223> n equals a,t,g, or c

<220>
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<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (69)
<223> n equals a,t,g, or c

<220>
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<222> (73)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (98)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (112)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (116)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (118)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (146)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (151)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (161)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (163)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (193)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (212)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (214)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (228)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (235)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (243)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (250)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (262)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (263)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (264)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (265)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (267)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (279)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (301)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (320)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (330)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (337)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (351)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (370)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (381)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (409)
<223> n equals a,t,g, or c

<400> 377
ggcacgagng tggctcnagg gngtcacctt cnntgttacc accgttnaca ccaaaagncg 60
gacngagana gtncagaagc tgtgcccagg ggggcagntc ccattcctgc tntatngnac 120
tgaagtgcac acagacacca acaagnttgc ngaatttctg nangcagtgc tgtgccctcc 180
caggtacccc aanctggcag ctctgaaccc tnantccaac acagctgngc tgganatatt 240
tgncaaattn tctgcctaca tnnnnanttc aaacccagna ctcaatgaca atctggagaa 300
nggactcctg aaagccctgn acgttttagn caattantta acatcccccc nctcagaaga 360
agtggatgan accagtgctg nagtgaaggt gtctctcaga agaagtttnt ggatagcacg 420
agctcáccct gggg 434

<210> 378
<211> 506
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (133)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (294)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (367)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (376)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (386)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (389)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (421)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (440)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (443)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (472)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (479)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (492)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (493)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (496)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (503)
<223> n equals a,t,g, or c

<400> 378
aattttcact cccctcagaa cataacatag taaatggatt gaattatgaa gaatggtttt 60
tatgcgactt accgcagcaa aaataaaggg aaagataagc gctcaataaa cctgtctgtt 120
ttccttaatt ctntgctggc tgataatcat cacctgcagg ttggctccaa ttatttgtat 180
attcataaaa tcgatggaaa aacttttctc tttaccaaaa caaatgacaa gagtctggtt 240
cagaagataa atcgctctaa agcttcagtt gaagatatta agaacagcct cgtngatgac 300
ggaatcattg ggattcccat ctttttgtt tgttgaaggc gacaccattg gtttttgcca 360
gaactgnttt tcgggncggc cacatncgnt tttgacaggt ttttttaatc ggggaaggga 420
ntgtccttaa ggcgtggggn gcngttcagt tggggccctg ttggggggac cnccaaggng 480
gtggttatgg cnnggntttc atnggc 506

<210> 379
<211> 550
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c

<400> 379
gacganacna accctcacta aagggaacaa aagctggagc tccaccgcgg tgcggccgct 60
ctagaactag tggatccccc gggctgcagg aattcggcac gaggccatcc agactgagga 120
agacccggaa acttaggggc cacgtgagcc acggccacgg ccgcataggc aagcaccgga 180
agcaccccgg cggccgcggt aatgctggtg gtctgcatca ccaccggatc aacttcgaca 240
aataccaccc aggctacttt gggaaagttg gtatgaagca ttaccactta aagaggaacc 300
agagcttctg cccaactgtc aaccttgaca aattgtggac tttggtcagt gaacagacac 360
gggtgaatgc tgctaaaaac aagactgggg ctgctcccat cattgatgtg gtgcgatcgg 420
gctactataa agttctggga aagggaaagc tcccaaagca gcctgtcatc gtgaaggcca 480
aattcttcag cagaagagct gaggagaaga ttaagagtgt tggggggcc tgtgtcctgg 540
tggcttgaag 550

<210> 380
<211> 573
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (4)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (10)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (160)
<223> n equals a,t,g, or c

<400> 380
aagncnagan agccaaccct cactaaaggg aacaaaagct ggagctccac cgcggtgcgg 60
ccgctctaga actagtggat cccccgggct gcaggaattc ggcacgagcg caaagaaggg 120
tggcgagaag aaaaagggcc gttctgccat caacgaaggn taacccgaga atacaccatc 180
aacattcaca agcgcatcca tggagtgggc ttcaagaagc gtgcacctcg ggcactcaaa 240
gagattcgga aatttgccat gaaggagatg ggaactccag atgtgcgcat tgacaccagg 300
ctcaacaaag ctgtctgggc caaaggaata aggaatgtgc cataccgaat ccgtgtgcgg 360
ctgtccagaa aacgtaatga ggatgaagat tcaccaaata agctatatac tttggttacc 420
tatgtacctg ttaccacttt caaaatttct gtgctaaaca gtgttacagt cgccaagagc 480
ccataaaggg agccctcctg gaagtggatg aggccttggg tctcggctct tcattgcttc 540
ctgagctgca gcagatgcct ttacaaccaa gct 573

<210> 381
<211> 531
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (5)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c

<400> 381
gcagnacnaa ccctcactaa agggaacaaa agctggagct ccaccgcggt gcggccgctc 60
tagaactagt ggatcccccg ggctgcagga attcggcacg aggcggcgtt ggcggcttgt 120
gcagcaatgg ccaagatcaa ggctcgagat cttcgcggga agaagaagga ggagctgctg 180
aaacagctgg acgacctgaa ggtggagctg tcccagctgc gcgtcgccaa agtgacaggc 240
ggtgcggcct ccaagctctc taagatccga gtcgtccgga aatccattgc ccgtgttctc 300
acagttatta accagactca gaaagaaaac ctcaggaaat tctacaaggg caagaagtac 360
aagcccctgg acctgcggcc taagaagaca cgtgccatgc gccgccggct caacaagcac 420
gaggagaacc tgaagaccaa gaagcagcag cggaaggagc ggctgtaccc gctgcggaag 480
tacgcggtca aggcctgagg ggcgcattgt caataaagca cagtggctga g 531

<210> 382
<211> 300
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (5)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (40)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (43)
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<220>
<221> misc feature
<222> (59)
<223> n equals a,t,g, or c

<220>
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<222> (171)
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<220>
<221> misc feature
<222> (172)
<223> n equals a,t,g, or c

<220>
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<223> n equals a,t,g, or c

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<222> (179)
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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (190)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (203)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (271)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (292)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (293)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (300)
<223> n equals a,t,g, or c

<400> 382
ngggngtacc acaaatataa ggcaaagagg aactgctggn cangagtacg gggtgtggnc 60
atgaatcctg tggagcatcc ttttggaggt ggcaaccacc agcacatcgg caagccctcc 120
accatccgca gagatgcccc tgctggccgc aaagtgggtc tcattgctgc nngcnggant 180
ggangtctcn ggggaaccaa gantgtgcag gagaaagaga actagtgctg agggcctcaa 240
taaagtttgt gtttatgcca aaaaaaaaaa naaaaaaaaa aaaaaaaaag annaaagagn 300

<210> 383
<211> 475
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (36)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (146)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (363)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (367)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (401)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (404)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (415)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (450)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (451)
<223> n equals a,t,g, or c

<400> 383
atgacgccgg tgcagcgggg gggcccgggg gcctgngtgg ccctgggatg gggaaccgcg 60
gtggcttccg cgaggtttcg gcagtggcat ccggggccgg ggtcgcggcc gtggacgggg 120
ccggggccga ggccgcggac tcgcgnaggc aaggccgagg ataaggagtg gatgcccgtc 180
accaagttgg gccgcttggt caaggacatg aagatcaagt ccctggagga gatctatctc 240
ttctccctgc ccattaagga atcagagatc attgattctt cctgggggct ctctcaagga 300
tgagttttga agatatgcca tgcagaagca gaccctgccg gccacgcacc agttcaagca 360
ttnttgnaac gggattaaat gccactcgtt tggtttaatg nccnagagtg gcacncatcc 420
tgggcaaaac tggcaaattt caagtccttn naagtatggg gaaaatggaa cccaa 475

<210> 384
<211> 127
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (5)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (8)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (31)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (62)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (71)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (103)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (124)
<223> n equals a,t,g, or c

<400> 384
caatntgnag accagattcc taaggctgca naggggacag tgggatctat tttaggaccg 60
angagattaa ncagagacac aggcaattgt atgtcagcag ctngatttaa cccacctaaa 120
aggngcg 127

<210> 385
<211> 317
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (30)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (151)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (187)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (203)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (231)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (264)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (308)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (311)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (316)
<223> n equals a,t,g, or c

<400> 385
ggcacgaggg atgtgcgacg tgtgcctggn gtagccccga ctcttgtacg gtcggcatct 60
gagaccagtg agaaacgccc cttcatgtgt gcttacccag gctgcaataa gagatatttt 120
aagctgtccc acttacagat gcacagcagg naagcacact ggtgagaaac cataccagtg 180
tgacttnaag gactgtgaac gangttttct cgttcagacc agctcaaaag ncaccaaagg 240
aggacataca ggtgtgaacc attnccagtg taaaattgtt cagcgaaatt ctcccggtcc 300
gaccaacnga ngaccna 317

<210> 386
<211> 433
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (295)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (311)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (359)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (385)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (405)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (407)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (427)
<223> n equals a,t,g, or c

<400> 386
tttcaaaagc tatttaggtg acactataga aggtagcctg caggttaccg gtccggaaat 60
tcccgggtcg acccacgcgt ccgccgagag ccttagccga cggaaactgg acactggaac 120
cggcagcgcc atgagactcc tccccсgctt gctgctgctt ctcttactcg tgttccctgc 180
cactgtcttg ttccgaggcg gccccagagg cttgttagca gtggcacaag atcttacaga 240
ggatgaagaa acagtagaag attccataat tgaggatgaa gatgatgaag ccgangtaga 300
agaagatgaa nccacagatt ttgtagaaga taaagaggaa gaagatgtgt ctggtgaanc 360
tgaaacttta ccgagtgcag atacnactat actgttttta aaggngnaga ttttccgcca 420
ataacantgt gaa 433

<210> 387
<211> 407
<212> DNA
<213> Homo sapiens

<220>
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<220>
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<222> (356)

<223> n equals a,t,g, or c

<220>
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<222> (359)
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<220>
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<222> (373)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (376)
<223> n equals a,t,g, or c

<220>
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<222> (407)
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<400> 387
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atttgaagca aacaggcagc gcgcgacaat ggcggtcgct cgtgcagctt tggggccatt 60
ggtgacgggt ctgtacgacg tgcaggcttt caagtttggg gacttcgtgc tgaagagcgg 120
gctttcctcc cccatctaca tcgatctgcg gggcatcgtg tctcgaccgc gtcttctgag 180
tcaggttgca gatattttat tccaaactgc ccaaaatgca ggcatcagtt ttgacaccgt 240
gtgtggagtg ccttatacag ctttgccatt ggctacagtt atctgttcaa ccaatcaaat 300
tccaatgctt attanaagga aagaaacaaa ggattatgga actaagcgtc ttgtanaang 360
aatattaatc canganaaac tgtttaatca ttgaaatgtt gtcccan              407
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<210> 388
<211> 244
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (215)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (221)
<223> n equals a,t,g, or c

<400> 388
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ttcgttcatc tatcggatcg ccacactcac aacaatgagt ggcagatata gcctggtggt 60
tcaggcggcg catttttatt gctgtgttgc gctgtaattc ttctatttct gatgctgaat 120
caatgatgtc tgccatcttt cattaatccc tgaactgttg gttaatacgc ttgagggtga 180
atgcgaataa taaaaaagga gcctgtagct ccctnatgat nttgcttttc atgttcatcg 240
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ttcc 244

<210> 389
<211> 239
<212> DNA
<213> Homo sapiens

<220>
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<220>
<221> misc feature
<222> (21)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (55)
<223> n equals a,t,g, or c

<220>
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<222> (64)
<223> n equals a,t,g, or c

<220>
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<222> (71)
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<220>
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<220>
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<222> (128)
<223> n equals a,t,g, or c

<220>
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<222> (163)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (185)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (196)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (202)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (205)
<223> n equals a,t,g, or c

<400> 389
nggactggcg tcagacgtcg nattccggcg cccacggtcg gcttaaaccc tggtncaatc 60
ctgncgcccg ncgtgatgcc agggaagaca gggcgacctg gaagtccaac tacttnctta 120
agatcatnca acgtattggg atgattatcc taaaatgggt tcnattggtg ggtagcgagt 180
acganatggt ggggcntcct anagntagta tggcgagcta gagtcccggc taatgttcc 239

<210> 390
<211> 382
<212> DNA
<213> Homo sapiens

<220>
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<220>
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<222> (54)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (69)
<223> n equals a,t,g, or c

<220>
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<222> (102)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (103)
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<220>
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<220>
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<222> (126)
<223> n equals a,t,g, or c

<220>
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<222> (169)
<223> n equals a,t,g, or c

<220>
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<222> (192)
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<220>
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<222> (217)
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<220>
<221> misc feature
<222> (219)
<223> n equals a,t,g, or c

<220>
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<222> (221)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (235)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (342)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (345)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (346)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (360)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (374)
<223> n equals a,t,g, or c

<400> 390
tcaangcgca attaaccctc actaaaggga acaaaagctg ggaacgatct ggtntctctg 60
cgcgctgcnc gcacactgag gccgcccggg acaaagcccg gnntcggngc gacctttggt 120
cccggnctca gtgagcgagc gagcgcgcag agagggagtg gccaacttna tcactagggg 180
ttccttgtag tnaatgatta acccgccatg ctacttngnc nacgtagcca tgggntacca 240
agctcgagct ctctagactc gacgcgcgta atacgactca ctatagggcg aatttgagct 300
ccaccgcggt tgcggccgct ctactagagt cgacctcatg gnttnncccc gaaacccgcn 360
aacacccgct gacncgccct ta 382

<210> 391
<211> 375
<212> DNA
<213> Homo sapiens

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<222> (6)
<223> n equals a,t,g, or c

<220>
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<222> (7)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (48)
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<220>
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<220>
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<222> (104)
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<220>
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<220>
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<220>
<221> misc feature
<222> (146)
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<220>
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<222> (159)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (208)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (223)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (261)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (269)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (275)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (279)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (299)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (351)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (366)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (370)
<223> n equals a,t,g, or c

<400> 391
tgcaanngaa tacacactaa ggacaagtgg actcacggtg cgccctcnga ctagtggtcc 60
cgggtgcagn tgccagggtg gcctgagcga tctacggatg ggcngtatgg agtggangag 120
acgagatgcg ggtgttanag cagggnctga ccggagtgnc acacatgagt gtcaggtgca 180
ggtagtccga gtcggcgaca tgagcctnga gtagagtcat cantcgatga gatctggagg 240
caactggcga gcaagaccgt ntggtgcant gtcantcang ctgttgcagg tgagagcant 300
gcactcgtcg agtggcgaga cagatcaatc tctgttagcg ggtggaggtt ncactcgcgc 360
tgtggnggtn cactg 375

<210> 392
<211> 121
<212> DNA
<213> Homo sapiens

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<222> (3)
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<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (13)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (56)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (67)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (113)
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<220>
<221> misc feature
<222> (118)
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<220>
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<222> (120)
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<400> 392
gantcatcng agngtgtgga tttgagccgc cgcatttttt aaccctaaat ctcganatgc 60
atcgtgnttc ctgtccattg gactgtaagg tttatgtagg catcttggga acnatggnan 120
a 121

<210> 393
<211> 83
<212> DNA
<213> Homo sapiens

<220>
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<222> (65)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (66)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (70)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (73)
<223> n equals a,t,g, or c

<400> 393
ggcagagaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60
aaaanncccn ggngggggcc ccc 83

<210> 394
<211> 218
<212> DNA
<213> Homo sapiens

<220>
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<222> (13)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (64)
<223> n equals a,t,g, or c

<400> 394
gtcggcgcag aangcgcccc gcacccccgc caggcgcatg tctgcacctc cgcttgccaa 60
aggncctcgg tcagcgactg gatgctcgcc atcaaggtcc agtggaagtt cttcaagagg 120
aaaggcgccc ccgccccagg cttccgcgcc cagcgctcgc cacgctcagt gcccgtttta 180
ccaataaact gagcgacccc aaaaaaaaaa aaaaaaag 218

<210> 395
<211> 83
<212> DNA
<213> Homo sapiens

<220>
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<222> (11)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (13)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (83)
<223> n equals a,t,g, or c

<400> 395
aattcggcac ngnaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60

aaaaaaaaaa aaaaaaaaaa aan 83

<210> 396
<211> 70
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (69)
<223> n equals a,t,g, or c

<400> 396
aattcggcac agaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60
aaaaaaaana 70

<210> 397
<211> 140
<212> DNA
<213> Homo sapiens

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<222> (57)
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<222> (74)
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<222> (93)
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<220>
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<220>
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<222> (114)
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<222> (115)
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<220>
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<222> (139)
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<400> 397
aatttgacca gagaacaaga ataacccggc ctcagcgccg ggttttcttn gcctcangat 60
cgcccccaaa acanataacc aattgtattt atngaaaaat aaatagatac aannnactaa 120
acatagcaat tcagatctnt 140

<210> 398
<211> 157
<212> DNA
<213> Homo sapiens

<220>
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<222> (10)
<223> n equals a,t,g, or c

<220>
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<222> (65)
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<220>
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<222> (121)
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<220>
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<222> (122)
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<220>
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<222> (123)
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<220>
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<222> (126)
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<220>

<221> misc feature
<222> (134)
<223> n equals a,t,g, or c

<220>
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<222> (150)
<223> n equals a,t,g, or c

<400> 398
aattcggcan agctcaagca gacggggctc aagggggtta catttaataa aaggatgaag 60
atggnaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120
nnnccngggg gggncccccc cccccctttn ccccctt 157

<210> 399
<211> 358
<212> DNA
<213> Homo sapiens

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<220>
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<222> (84)
<223> n equals a,t,g, or c

<220>
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<222> (204)
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<220>
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<222> (207)
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<222> (302)
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<220>
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<222> (305)
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<220>
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<222> (308)
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<220>
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<222> (331)
<223> n equals a,t,g, or c

<220>
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<222> (341)
<223> n equals a,t,g, or c

<400> 399
ggcanagcgg cagaggcggc tcccactctc ggaaccttgt cctgtttttc ccccagctcg 60
gcaagcgcca tatgagcctg gcgncgccaa tagcgaatcc tgttgtgggc tttttggcct 120
attcccgccc ctcagtcttg ccgggatggc accgcccgca taggacttcc agggttgggc 180
tgagtgggag ttcgactgct gggnctngta attctcgctt tgggggctgc tccttccagg 240
ctggggacac actggggccc gttgttcggt ctcccgtcct ccgacatctt gtctggaact 300
tncgnctngc agtttccata ggagttggag nctgtgcggc ntaattttgg tggaaaaa 358

<210> 400
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<212> DNA
<213> Homo sapiens

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<220>
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<220>
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<222> (213)
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<220>
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<220>
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<222> (218)
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<220>
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<222> (231)
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<220>
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<222> (239)
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<220>

<221> misc feature
<222> (245)
<223> n equals a,t,g, or c

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<220>
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<222> (262)
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<220>
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<222> (269)
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<220>
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<222> (279)
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<220>
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<222> (283)
<223> n equals a,t,g, or c

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<220>
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<222> (316)
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<220>
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<220>
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<222> (349)
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<220>
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<220>
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<222> (382)
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<400> 400
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aaaacccaan tcagagtatc canaaatcca agccaggtca aaaccaaaac gaaantntca 120
agcaatccaa atcaagtcaa aaacaaaaac caaagtgccg gtacaggcnt nccgtgggtg 180
atcaggccac ccttccactc aaatggagtg ggnaantncc aaagactagt nttaccaant 240
ttcanatntc cggantccaa gngcctgtnc cttcccagng ttnagccgct gnattgatcc 300
tctgtggggg cctgcnaaac gccantctgg cgaggtgttc cactggggna attgcctacc 360
cggnagtgct ctcaggttct gngtccctca agctggcca                        399
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<210> 401
<211> 189
<212> DNA
<213> Homo sapiens

<220>
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<220>
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<222> (11)
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<220>
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<222> (162)
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<221> misc feature
<222> (166)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (187)
<223> n equals a,t,g, or c

<400> 401
naattcggca nagcaaacca caccttctct ttcttatgtc tttttactac aaactacaag 60
acaattgttg aaacctgcta tacatgttta ttttaataaa ttgatggcaa aaaaaaaaaa 120
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa anccnngggg ggggcccccc 180
cccccccntt 189

<210> 402
<211> 174
<212> DNA
<213> Homo sapiens

<220>
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<222> (10)
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<220>
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<222> (73)
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<220>
<221> misc feature
<222> (103)
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<220>
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<220>
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<222> (130)
<223> n equals a,t,g, or c

<220>
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<222> (132)
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<220>
<221> misc feature
<222> (146)
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<220>
<221> misc feature
<222> (149)
<223> n equals a,t,g, or c

<220>
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<222> (167)
<223> n equals a,t,g, or c

<400> 402
aattcggcan agctgaggca ggagaatcgc ttgaattcgg gaggcagagc tgagatcaca 60
cctctgacac tcnagcctgg gtgacagagc gagactccgt ctnaggnaag gaaaaaaaaa 120
aaaaaaaaan cncggggggg gccccngtnc ccaattggcc ctatagnggg tcgt 174

<210> 403
<211> 263
<212> DNA
<213> Homo sapiens

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<220>
<221> misc feature
<222> (231)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (236)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (242)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (252)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (260)
<223> n equals a,t,g, or c

<400> 403
ggcanagcca acccagcagt ccttccctca gctgcctagg aggaagggac ccagctgggt 60
ctgggaccac aagggaggag actgcacccc actgcctctg ggccctggct gtgggcagag 120
gccaccgtgt gtgtcccgag taaccgtgcc gttgtcgtgt gatgccataa gcgtctgtgc 180
gtggagtccc caatgaaacc tgtggtcctg cctgggcaaa aaaaaaaaaa naaaanaaaa 240
anaaagaaaa anaaaaaaan aaa 263

<210> 404
<211> 478
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (159)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (259)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (427)
<223> n equals a,t,g, or c

<400> 404
tcgacccacg cgtccggggg ctgcagcatg ttgctgagga gtgaggaata gttgagcccc 60
aagtcctgaa gaggcgggcc agccaggctg acatctgtgt ttcaagtggg gctcgccatg 120
ccgggggttc ataggtcact ggctctccaa gtgccagang tgggcaggtg gtggcactga 180
gcccccccaa cactgtgccc tggtggagaa agcactgacc tgtcatgccc ccctcaaacc 240
tcctcttctg acgtgcctnt tgcacccctc ccattaggac aatcagtccc ctcccatctg 300
ggagtcccct tttcttttct accctagcca ttcctggtac ccagccatct gcccaagggt 360
gccccctcct ctcccatccc cctgccctcg tgggcagccc ggctggtttt gtaaatgtgg 420
gttgtgnaca gtgatttttt cttgtattta aaaaaggcca gcattgtggt tcattaaa 478

<210> 405
<211> 223
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (147)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (158)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (172)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (217)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (223)
<223> n equals a,t,g, or c

<400> 405
agacagcagg acggtggcca tggaagtcgg aatccgctaa ggagtgtgta acaactcacc 60
tgccgaatca actagccctg aaaatggatg gcgctggagc gtcgggccca tacccgtccg 120
tcgccggcag tcgagagtgg acgggancgg cgggggcngc gcgcgcgcgc gncgtgatgg 180
tgtgcgtcgg agggcggcgg cggcggcggg ggtgtgnggt ccn 223

<210> 406
<211> 104
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (37)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (81)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (93)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (103)
<223> n equals a,t,g, or c

<400> 406
cccacgcntc cgccgacagc agcagcctca ccatgangtt gctgatggtc ctcatgctgg 60
cggccctctc ccagcactgc nacgcaggct ctngctgccc ctna 104

<210> 407
<211> 66
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (17)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (21)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (57)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (66)
<223> n equals a,t,g, or c

<400> 407
gccctatagt gagtctngta ncaattcact ggccgtcgtt ttacaacgtc gtgacgngga 60
aaactn 66

<210> 408
<211> 278
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (19)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (252)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (275)
<223> n equals a,t,g, or c

<400> 408
gggcanagca agctcctgna cctcaagtga tccacatgcc ttggttgacc aaattgctgg 60
gattacaggc atgagccaat atgaccagct caaacatctt ctttttaaat gtcagaagca 120
tgtatagtga ttatttctta ttttttcccc cttgatccat ctcaccagat gtttgttgat 180
tttataagaa ttttcaaact accagcttct ggctttgttg aacttgggat ttctgtttca 240
ctaattttct tnctcctgtc ttgtacttac tttgntgg 278

<210> 409
<211> 168
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (16)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (38)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (127)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (140)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (143)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (145)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (167)
<223> n equals a,t,g, or c

<400> 409
aataaaactc taaaangatc actataaaaa aagcaggnac gcctgcaggt accggtccgg 60
aattcccggg tcgacccacg cgtccgacgg ctgcgagaag acgacagaag ggcacggctg 120
cgagaanacg acagaagggn gcnantgaaa gaaggcggca gaaaggnt 168

<210> 410
<211> 415
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (307)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (347)
<223> n equals a,t,g, or c

<400> 410
tgaataccta agatttctgt cttggggttt ttggtgcatg cagttgatta cttcttattt 60
ttcttaccaa ttgtgaatgt tggtgtgaaa caattaatga agcttttgaa tcatccctat 120
tctgtgtttt atctagtcac ataaatggat taattactaa tttcagttga gaccttctaa 180
ttggttttta ctgaaacatt gagggaacac aaatttatgg gcttcctgat gatgattctt 240
ctaggcatca tgtcctatag tttgtcatcc ctgatgaatg taaaattaca ctgttcacaa 300
aggtttngtc tcctttccac tgctattaat catggtcact ctccccnaaa tattatattt 360
tttctattaa aagaaaaaaa tggaaaaaaa ttacaaggca atggaaacta ttata 415

<210> 411
<211> 636
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (383)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (512)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (519)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (544)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (547)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (583)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (599)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (603)
<223> n equals a,t,g, or c

<400> 411
gcagatcaga cgtggcgacc cgctgaattt aagcatatta gtcagcggag gagaagaaac 60
taaccaggat tccctcagta acggcgagtg aacagggaag agcccagcgc cgaatccccg 120
ccccgcggcg gggcgcggga catgtggcgt acggaagacc cgctccccgg cgccgctcgt 180
ggggggccca agtccttctg atcgaggccc agcccgtgga cggtgtgagg ccggtagcgg 240
cccccggcgc gccgggcccg ggtcttcccg gagtcgggtt gcttgggaat gcagcccaaa 300
gcgggtggta aactccatct aaggctaaat ccccttgtaa atttaactgt tagtccaaag 360
aggaacagct ctttggacac tangaaaaaa ccttgtagag agagtaaaaa atttaacacc 420
catagtaggc ctaaaagcag ccaccaatta agaaagcgtt caagctcaac acccactacc 480
taaaaaatcc caaacatata actgaactcc tnacacccna ttggaccaat ctatcaccct 540
atanaanaac taatggtagt ataagtaaca tgaaaacatt ctncttcgca taagcctgng 600
tanattaaaa cacttgaact gaccattaac aggcca 636

<210> 412
<211> 182
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (129)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (166)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (169)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (170)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (172)
<223> n equals a,t,g, or c

<400> 412
ccattgattt ttatcaatag tcgtattcat acggatagtc ctggtattgt tccatcacat 60
tctgaggatg ctcttcgaac tcttcaaatt cttcttccat atatcacctt aaatagtgga 120
ttgcggtant aaagattgtg cctgtctttt aaccacatca ggctcngann gntctcgtga 180
ac 182

<210> 413
<211> 387
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (157)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (253)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (317)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (323)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (349)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (351)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (364)
<223> n equals a,t,g, or c

<400> 413
tcgacccacg cgtccgccca cgcgtccgcc aagaccaccc tcctttcatt tgctagaagg 60
actcactaga ctcaggaaag ctgttaggct cacagttaca gtttattaca gtaaaaggac 120
agagattaag atcagcaaag ggaggaggtg cacagcnacg ttccacgaca gatgaggcga 180
cggcttccat ctgccctctc ccagtggagc catataggca gcacctgatt ctcacagcaa 240
catgtgacaa canccaagaa gtactgccaa tactgccaac cagagcagct tcactcggag 300
atctttgtgt tccaganttt ttngtttgtc ttggagacag ggtctgggnc ngtttgggca 360
gacnaagagt acatggtgga gattcac 387

<210> 414
<211> 276
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (60)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (186)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (195)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (237)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (260)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (266)
<223> n equals a,t,g, or c

<400> 414
gcaaaggtcc atactggtta cttggtttca ttgccaccac ttagtggatg ttcagtttan 60
aaccattttg tctgctccct ctggaagcct tgcgcatagc ttactttgta attgttggag 120
aataactgct gaatttttag ctgttttgag ttgattcgca ccactgcacc acaactcact 180
atgaanacta tttancttat ttattatctt gtgaaaagta taccatgaaa attttgntca 240
tactgtattt atcaagtatn attaanagca ctagat 276

<210> 415
<211> 192
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (78)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (88)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (99)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (145)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (150)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (164)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (168)
<223> n equals a,t,g, or c

<400> 415
aaaagattgg actaagacac tggccatacc actggacagg gttatgttaa cacctgaaat 60
tgctgggtct tgagagancc caacgcantt ctgggagang gaccacattg gggggtaggt 120
ccacgggctt ggtgatagaa ttatntctcn atcgacttct tgantgcnat atgaactgta 180
acatttgctt ag 192

<210> 416
<211> 439
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (7)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (64)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (406)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (417)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (421)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (431)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (434)
<223> n equals a,t,g, or c

<400> 416
gcgagantnc gacagaaggg tacggctgcg agagacgaca gaagggtacg gctgcgagaa 60
gacnacagaa gggtacggct gcgagaagac gacagaaggg tacggctgcg agaagacgac 120
agaagggtac ggctgcgaga agacgacaga aggtacggct gcgagaagac gacagaagga 180
tacggctgcg agaagacgac agaagggaga atcttagttc aactttaaat ttgcccacag 240
aaccctctaa atccccttgt aaatttaact gttagtccaa agaggaacag ctctttggac 300
actaggaaaa aaccttgtag agagagtaaa aaatttaaca cccatagtag gcctaaaagc 360
agccaccaat taagaaagcg ttcaaagctc aacacccact acccanaaaa taaaaanaaa 420
naaaaacccg nggnccgct 439

<210> 417
<211> 155
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (84)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (122)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (123)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (143)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (153)
<223> n equals a,t,g, or c

<400> 417
gacatcttnt tggtttttat tttgaaacaa tttttaggct tgttccgggg gtctctgtgc 60
tgcctgtact gtattgacct gttntatagg tgccttttta ttaaaaagaa aattcaaaaa 120

annaaaaaaa aaattaataa aanaaaaaaa aanca 155

<210> 418
<211> 291
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (285)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (286)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (288)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (289)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (291)
<223> n equals a,t,g, or c

<400> 418
gaaaaaagaa atccatatct taaagaaaca gctttcaagt gcctttctgc agtttttcag 60
gagcgcaaga tagatttgga ataggaataa gctctagttc ttaacaaccg acactcctac 120
aagatttaga aaaaagttta caacataatc tagtttacag aaaaatcttg tgctagaata 180
ctttttaaaa ggtattttga ataccattaa aactgctttt ttttttccag caagtatcca 240
accaacttgg ttctgcttca ataaatcttt ggaaaaacta atttnnanna n 291

<210> 419
<211> 340
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (315)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 419
Val Xaa Asp Trp Phe Leu Trp Tyr Val Lys Lys Cys Gly Gly Thr Thr
1 5 10 15

Arg Ile Ile Ser Thr Thr Asn Gly Gly Gln Glu Arg Lys Phe Val Gly
20 25 30

Gly Ser Gly Gln Val Ser Glu Arg Ile Met Asp Leu Leu Gly Asp Arg
35 40 45

Val Lys Leu Glu Arg Pro Val Ile Tyr Ile Asp Gln Thr Arg Glu Asn
50 55 60

Val Leu Val Glu Thr Leu Asn His Glu Met Tyr Glu Ala Lys Tyr Val
65 70 75 80

Ile Ser Ala Ile Pro Pro Thr Leu Gly Met Lys Ile His Phe Asn Pro
85 90 95

Pro Leu Pro Met Met Arg Asn Gln Met Ile Thr Arg Val Pro Leu Gly
100 105 110

Ser Val Ile Lys Cys Ile Val Tyr Tyr Lys Glu Pro Phe Trp Arg Lys
115 120 125

Lys Asp Tyr Cys Gly Thr Met Ile Ile Asp Gly Glu Glu Ala Pro Val
130 135 140

Ala Tyr Thr Leu Asp Asp Thr Lys Pro Glu Gly Asn Tyr Ala Ala Ile
145 150 155 160

Met Gly Phe Ile Leu Ala His Lys Ala Arg Lys Leu Ala Arg Leu Thr
165 170 175

Lys Glu Glu Arg Leu Lys Lys Leu Cys Glu Leu Tyr Ala Lys Val Leu
180 185 190

Gly Ser Leu Glu Ala Leu Glu Pro Val His Tyr Glu Glu Lys Asn Trp
195 200 205

Cys Glu Glu Gln Tyr Ser Gly Gly Cys Tyr Thr Thr Tyr Phe Pro Pro
210 215 220

Gly Ile Leu Thr Gln Tyr Gly Arg Val Leu Arg Gln Pro Val Asp Arg
225 230 235 240

Ile Tyr Phe Ala Gly Thr Glu Thr Ala Thr His Trp Ser Gly Tyr Met
245 250 255

Glu Gly Ala Val Glu Ala Gly Glu Arg Ala Ala Arg Glu Ile Leu His
260 265 270

Ala Met Gly Lys Ile Pro Glu Asp Glu Ile Trp Gln Ser Glu Pro Glu
275 280 285

Ser Val Asp Val Pro Ala Gln Pro Ile Thr Thr Thr Phe Leu Glu Arg
290 295 300

His Leu Pro Ser Val Pro Gly Leu Leu Arg Xaa Ile Gly Leu Thr Thr
305 310 315 320

Ile Phe Ser Ala Thr Ala Leu Gly Phe Leu Ala His Lys Arg Gly Leu
325 330 335

Leu Val Arg Val
340

<210> 420
<211> 111
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 420
Thr Arg Asp Leu Val Ser Phe Ile Ser Gly Ile Arg Leu Tyr Asn Leu
1 5 10 15

Met Leu Ser Val Leu Arg His Lys Arg Gln Asn Val Ala Tyr Phe Arg
20 25 30

Ile Cys Phe Phe Ile Glu Val Ser Gly Ile Leu Ser Lys Ile Val Xaa
35 40 45

Ser Arg His Cys Ser Leu Cys Ser Ser Gly Thr Ser Cys Pro Leu Leu
50 55 60

Ser Leu Gln Ala Thr Gly Asn Ala Ser Val Leu Val Ser Trp Arg Lys
65 70 75 80

Ile Thr Trp Gly Glu Gly Thr Ser Cys Gly Lys Ser Lys Cys Arg Tyr
85 90 95

Glu Met Arg Arg Leu Pro Gln Leu Lys Val Asp Lys Ser Ala Leu

100 105 110

<210> 421
<211> 61
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 421
Xaa Ile Trp Cys Ile Ile Cys Lys Glu Ser Lys Met Met Ser Phe Pro
1 5 10 15

Arg Gly Met Asn Leu Arg Asn Ala Phe Asp Gly Asp Val Ser Val Thr
20 25 30

Leu Cys Tyr Ser Gly Ser Ser Asn Asn Ser Lys Ala Asn Tyr Ser Lys
35 40 45

Cys Lys Ile Phe Leu Phe Pro Arg Phe Thr Phe Val Trp
50 55 60

<210> 422
<211> 51
<212> PRT
<213> Homo sapiens

<400> 422
Thr His Ala Tyr Cys Ser Asn Leu Ser Phe Arg Leu Tyr Asp Gln Trp
1 5 10 15

Arg Ala Trp Met Gln Lys Ser His Lys Thr Arg Asn Gln His Arg Thr
20 25 30

Arg Gly Ser Cys Pro Arg Ala Asp Gly Ala Arg Arg Glu Val Leu Pro
35 40 45

Asp Lys Leu
50

<210> 423
<211> 246

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (71)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (101)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (117)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (147)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 423
Thr Arg Asn Asp Met Lys Ala Asp Cys Ile Leu Tyr Tyr Gly Phe Gly
1 5 10 15

Asp Ile Phe Arg Ile Ser Ser Met Val Val Met Glu Asn Val Gly Gln
20 25 30

Gln Lys Leu Tyr Glu Met Val Ser Tyr Cys Gln Asn Ile Ser Lys Cys
35 40 45

Arg Arg Val Leu Met Ala Gln His Phe Asp Glu Val Trp Asn Ser Glu
50 55 60

Ala Cys Asn Lys Met Cys Xaa Asn Cys Cys Lys Asp Ser Ala Phe Glu
65 70 75 80

Arg Lys Asn Ile Thr Glu Tyr Cys Arg Asp Leu Ile Lys Ile Leu Lys
85 90 95

Gln Ala Glu Gly Xaa Gly Met Glu Lys Leu Thr Pro Ile Gly Asn Trp
100 105 110

Ile Asp Ser Trp Xaa Gly Lys Gly Ala Ala Lys Leu Arg Val Ala Gly
115 120 125

Val Val Ala Pro Thr Leu Pro Arg Glu Asp Leu Glu Lys Ile Ile Ala
130 135 140

His Phe Xaa Ile Gln Gln Tyr Leu Lys Glu Asp Tyr Ser Phe Thr Ala
145 150 155 160

Tyr Ala Thr Ile Ser Tyr Leu Lys Ile Gly Pro Lys Ala Asn Leu Leu
165 170 175

Asn Asn Glu Ala His Ala Ile Thr Met Gln Val Thr Lys Ser Thr Gln
180 185 190

Asn Ser Phe Arg Ala Glu Ser Ser Gln Thr Cys His Ser Glu Gln Gly
195 200 205

Asp Lys Lys Met Glu Glu Lys Asn Ser Gly Asn Phe Gln Lys Lys Ala
210 215 220

Ala Asn Met Leu Gln Gln Ser Gly Ser Lys Asn Thr Gly Ala Lys Lys
225 230 235 240

Arg Lys Ile Asp Asp Ala
245

<210> 424
<211> 109
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (77)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 424
Asp His Trp Pro Arg Pro Glu Trp Leu Pro Cys Thr Ser Trp Arg Arg
1 5 10 15

Ala Ser Cys Leu Asn His Val Asn Cys His His Leu Ala Thr Pro Ala
20 25 30

Pro Ala Ser Ala Leu Pro Pro Phe Pro Pro Ser Trp Ser Gly Gly Tyr
35 40 45

Arg Ser Leu Gly Pro Thr Leu Ala Pro Leu Ser Pro Ala Ser Val Cys
50 55 60

Leu Thr Val Phe Pro Pro Leu Pro Gln Leu Arg Cys Xaa Pro Gln Ala
65 70 75 80

Trp Cys Cys Leu Gly Gly Leu Gly Glu Gly Val Cys Gly Gly Gly Arg
85 90 95

Arg Val Lys Thr Glu Ala Arg Cys Gln Asn Gly Leu Glu
100 105

<210> 425
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 425
Gly Ser Glu Thr Xaa Lys Tyr Leu Val Glu Asp Lys Arg Leu Gly Leu
1 5 10 15

Tyr Thr Trp Leu Cys Thr Asp Leu Leu Ser His Ile Gly Asn His His
20 25 30

Thr Leu Gln Gly Ile Ser Phe Ile Cys Lys Met Gln Arg Leu Val Leu
35 40 45

Xaa Asn His Thr Asn Phe Phe Val Leu
50 55

<210> 426
<211> 99
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (96)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 426
Phe Gly Thr Ser Gly Asp Gly Gly Gly Ser Lys Met Ala Gln Ala Ile
1 5 10 15

Phe Glu Ala Leu Glu Gly Met Asp Asn Gln Thr Val Leu Ala Val Gln

20 25 30

Ser Leu Leu Asp Gly Gln Gly Ala Val Pro Asp Pro Thr Gly Gln Ser
35 40 45

Val Asn Ala Pro Pro Ala Ile Gln Pro Leu Asp Asp Glu Asp Val Phe
50 55 60

Leu Cys Gly Lys Cys Lys Lys Gln Phe Asn Ser Leu Pro Ala Phe Met
65 70 75 80

Thr His Lys Arg Glu Gln Cys Gln Gly Asn Ala Pro Ala Leu Ala Xaa
85 90 95

Val Ser Leu

<210> 427
<211> 55
<212> PRT
<213> Homo sapiens

<400> 427
Asn Ser Asn Ser Ser Ile Phe Ser Leu Val Ser Val Lys Cys Asp Lys
1 5 10 15

Ser Thr Tyr Phe Lys Leu Phe Ser Ala Leu Gly Tyr Ser Ser Asn Lys
20 25 30

Asn Thr Asn Leu Trp Val Phe Lys Lys Thr Trp Arg Ile Asn Ser Tyr
35 40 45

Phe Lys Arg Ser Lys Lys Lys
50 55

<210> 428
<211> 54
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 428
His Thr Leu Ser Asn Leu Glu Phe Ala Gln Lys Val Glu Pro Cys Asn

```
1               5                   10                  15

Asp His Val Arg Ala Lys Leu Ser Trp Ala Lys Lys Arg Asp Glu Asp
            20                  25                  30

Asp Val Pro Thr Val Pro Ser Thr Xaa Gly Glu Glu Arg Leu Tyr Asn
        35                  40                  45

Pro Phe Leu Arg Val Ala
    50



&lt;210&gt; 429
&lt;211&gt; 39
&lt;212&gt; PRT
&lt;213&gt; Homo sapiens

&lt;400&gt; 429
Arg Gln Thr Lys Val Asn Leu Lys Glu Thr Arg Ser Phe Glu Ile Ile
  1               5                   10                  15

Val Trp Gly Phe Tyr Lys Ser Asn Tyr Cys His Leu His Pro Asp Ser
            20                  25                  30

Phe Lys Leu Leu Ile His Pro
        35



&lt;210&gt; 430
&lt;211&gt; 133
&lt;212&gt; PRT
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; SITE
&lt;222&gt; (81)
&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;
&lt;221&gt; SITE
&lt;222&gt; (85)
&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 430
Ala Arg Ala Pro Arg Val Pro Pro Ala Pro His Thr Pro Ser Lys Met
  1               5                   10                  15

Gly Lys Glu Lys Thr His Ile Asn Ile Val Val Ile Gly His Val Asp
            20                  25                  30
```

Ser Gly Lys Ser Thr Thr Thr Gly His Leu Ile Tyr Lys Cys Gly Gly
35 40 45

Ile Asp Lys Arg Thr Ile Glu Lys Phe Glu Lys Glu Ala Ala Glu Met
50 55 60

Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys Ala
65 70 75 80

Xaa Val Ser Ala Xaa Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe Glu
85 90 95

Thr Thr Lys Tyr Tyr Ile Thr Ile Ile Asp Ala Pro Gly His Arg Asp
100 105 110

Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala Val
115 120 125

Leu Ile Val Ala Ala
130

<210> 431
<211> 190
<212> PRT
<213> Homo sapiens

<400> 431
Leu Cys Trp Ala Arg Pro Leu Pro Ser Gly Pro Val Leu Leu Ala Ala
1 5 10 15

Asn Lys Asp Ser Ser Trp Cys Pro Thr Cys Leu Val His Cys Cys Val
20 25 30

Asn Pro Gly Gly Ser Gly His Arg Arg Gln Pro Arg Pro Arg Val Gln
35 40 45

Glu Lys Cys Ser Leu Glu Ala Arg Thr Thr Ala Ser His Trp Gly Arg
50 55 60

Arg Gly Pro Arg Thr Thr Ser Ala Ser Tyr Leu Pro Ala Ser Ala Arg
65 70 75 80

Gly Pro Arg Asp Ala Val Leu Phe Gln Pro Pro Ala Leu Gly Arg Gly
85 90 95

His Ala Ser Arg Ile Gln Gly Ala Gly Gly Leu Ser Thr Ala Arg Thr
100 105 110

Cys Leu Leu Ala Ala Ala Ala Val Gly Glu His Gly Gly Cys Gln Arg
        115   120   125

Leu Leu Trp Lys Val Ala Ala Ser Glu Met Ala Gly Ala Ala Gly Val
    130   135   140

Arg Leu His Thr Ala Gln Val Ser Ser Gly Arg Leu Ser Trp Gly Gly
145   150   155   160

Ser Ser Ser Ala Glu Gly Trp Trp Gly Val Gln Ser Val Ile Leu Gly
                165   170   175

Ala Val Cys Pro Thr Pro Ala Trp Gly Pro His Phe Arg Arg
            180   185   190

<210> 432
<211> 310
<212> PRT
<213> Homo sapiens

<400> 432
Gly Pro His Gly Asn Gly Glu Val Arg Trp Pro Leu Pro Pro Pro Pro
 1   5   10   15

Pro Arg Phe Val Ala Arg Arg Lys Met Ala Asp Leu Glu Glu Gln Leu
            20   25   30

Ser Asp Glu Glu Lys Val Arg Ile Ala Ala Lys Phe Ile Ile His Ala
        35   40   45

Pro Pro Gly Glu Phe Asn Glu Val Phe Asn Asp Val Arg Leu Leu Leu
    50   55   60

Asn Asn Asp Asn Leu Leu Arg Glu Gly Ala Ala His Ala Phe Ala Gln
65   70   75   80

Tyr Asn Leu Asp Gln Phe Thr Pro Val Lys Ile Glu Gly Tyr Glu Asp
                85   90   95

Gln Val Leu Ile Thr Glu His Gly Asp Leu Gly Asn Gly Lys Phe Leu
            100   105   110

Asp Pro Lys Asn Arg Ile Cys Phe Lys Phe Asp His Leu Arg Lys Glu
        115   120   125

Ala Thr Asp Pro Arg Pro Cys Glu Val Glu Asn Ala Val Glu Ser Trp
    130   135   140

Arg Thr Ser Val Glu Thr Ala Leu Arg Ala Tyr Val Lys Glu His Tyr

145 150 155 160

Pro Asn Gly Val Cys Thr Val Tyr Gly Lys Lys Ile Asp Gly Gln Gln
165 170 175

Thr Ile Ile Ala Cys Ile Glu Ser His Gln Phe Gln Ala Lys Asn Phe
180 185 190

Trp Asn Gly Arg Trp Arg Ser Glu Trp Lys Phe Thr Ile Thr Pro Ser
195 200 205

Thr Thr Gln Val Val Gly Ile Leu Lys Ile Gln Val His Tyr Tyr Glu
210 215 220

Asp Gly Asn Val Gln Leu Val Ser His Lys Asp Ile Gln Asp Ser Leu
225 230 235 240

Thr Val Ser Asn Glu Val Gln Thr Ala Lys Glu Phe Ile Lys Ile Val
245 250 255

Glu Ala Ala Glu Asn Glu Tyr Gln Thr Ala Ile Ser Glu Asn Tyr Gln
260 265 270

Thr Met Ser Asp Thr Thr Phe Lys Ala Leu Arg Arg Gln Leu Pro Val
275 280 285

Thr Arg Thr Lys Ile Asp Trp Asn Lys Ile Leu Ser Tyr Lys Ile Gly
290 295 300

Lys Glu Met Gln Asn Ala
305 310

<210> 433
<211> 289
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (287)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (288)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 433
Gln Ser Cys Thr Ser Gly Ser Ser Lys Pro Asn Ser Pro Ser Ile Ser

```
1               5                   10                  15

Pro Ser Ile Leu Ser Asn Thr Glu His Lys Arg Gly Pro Glu Val Thr
            20                  25                  30

Ser Gln Gly Val Gln Thr Ser Ser Pro Ala Cys Lys Gln Glu Lys Asp
        35                  40                  45

Asp Lys Glu Glu Lys Lys Asp Ala Ala Glu Gln Val Arg Lys Ser Thr
    50                  55                  60

Leu Asn Pro Asn Ala Lys Glu Phe Asn Pro Arg Ser Phe Ser Gln Pro
65                  70                  75                  80

Lys Pro Ser Thr Thr Pro Thr Ser Pro Arg Pro Gln Ala Gln Pro Ser
                85                  90                  95

Pro Ser Met Val Gly His Gln Gln Pro Thr Pro Val Tyr Thr Gln Pro
            100                 105                 110

Val Cys Phe Ala Pro Asn Met Met Tyr Pro Val Pro Val Ser Pro Gly
        115                 120                 125

Val Gln Pro Leu Tyr Pro Ile Pro Met Thr Pro Met Pro Val Asn Gln
    130                 135                 140

Ala Lys Thr Tyr Arg Ala Gly Lys Val Pro Asn Met Pro Gln Gln Arg
145                 150                 155                 160

Gln Asp Gln His His Gln Ser Ala Met Met His Pro Ala Ser Ala Ala
                165                 170                 175

Gly Pro Pro Ile Ala Ala Thr Pro Pro Ala Tyr Ser Thr Gln Tyr Val
            180                 185                 190

Ala Tyr Ser Pro Gln Gln Phe Pro Asn Gln Pro Leu Val Gln His Val
        195                 200                 205

Pro His Tyr Gln Ser Gln His Pro His Val Tyr Ser Pro Val Ile Gln
    210                 215                 220

Gly Asn Ala Arg Met Met Ala Pro Pro Thr His Ala Gln Pro Gly Leu
225                 230                 235                 240

Val Ser Ser Ser Ala Thr Gln Tyr Gly Ala His Glu Gln Thr His Ala
                245                 250                 255

Met Tyr Ala Cys Pro Lys Leu Pro Tyr Asn Lys Glu Thr Ser Pro Ser
            260                 265                 270

Phe Tyr Phe Ala Ile Ser Thr Gly Ser Leu Ala Gln Gln Tyr Xaa Xaa
```

275 280 285

Pro

<210> 434
<211> 147
<212> PRT
<213> Homo sapiens

<400> 434
Lys Val Thr Pro Asp Leu Lys Pro Thr Glu Ala Ser Ser Ser Ala Phe
1 5 10 15

Arg Leu Met Pro Ala Leu Gly Val Ser Val Ala Asp Gln Lys Gly Lys
20 25 30

Ser Thr Val Ala Ser Ser Glu Ala Lys Pro Ala Ala Thr Ile Arg Ile
35 40 45

Val Gln Gly Leu Gly Val Met Pro Pro Lys Ala Gly Gln Thr Ile Thr
50 55 60

Val Ala Thr His Ala Lys Gln Gly Ala Ser Val Ala Ser Gly Ser Gly
65 70 75 80

Thr Val His Thr Ser Ala Val Ser Leu Pro Ser Met Asn Ala Ala Val
85 90 95

Ser Lys Thr Val Ala Val Ala Ser Gly Ala Ala Arg Pro Pro Ser Ala
100 105 110

Ser Ala Gln Glu Pro Pro Pro Cys Gly Arg Ser Leu Ser Ala Pro Arg
115 120 125

Leu Cys Pro Arg Pro Arg Leu Gly Ser Cys Leu His Gly Ser Gln Phe
130 135 140

Pro Ser Leu
145

<210> 435
<211> 151
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (79)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 435
Gly Ser Gly Thr Lys Asp Pro Ser Xaa Cys Asn Thr Gln Thr Xaa Ala
1 5 10 15

His Thr His Thr Gly Gly Glu Ile Ser Leu Phe Ser Met Ser Phe Phe
20 25 30

Ser Trp Ala Glu Thr Gly Tyr Cys Pro Gly Gln Leu Pro Glu Lys His
35 40 45

Arg Arg Glu Leu Arg Ser Ala Arg Pro Ser Ser Leu Ala Pro Gly Phe
50 55 60

Gly Gly Pro Arg Thr Ala Asp Arg Gly Trp Ser Trp Arg Leu Xaa Ser
65 70 75 80

Arg Ala Tyr Thr Trp Arg Asn Ala Pro Pro Ser Ser Pro Ser Leu Gln
85 90 95

Thr Trp Gly Trp Leu Gly Pro Glu Gly Cys Asp Glu Glu Lys Arg Ala
100 105 110

Ser Val Gly Met Arg Gln Glu Gly Ile Asp Phe Asp Cys Asp Leu Trp
115 120 125

Gly Phe Leu Pro Ala Leu Asp Asn Pro Ala Lys Asp Cys Phe Phe Leu
130 135 140

Ser Leu Ala Arg Arg Gly Pro
145 150

<210> 436
<211> 180
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (123)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 436
```
Ala Pro Ala Ser Pro Val Met Pro Pro Gln Thr Gln Ser Pro Gly Gln
  1               5                  10                  15

Pro Ala Gln Pro Ala Pro Met Val Pro Leu His Gln Lys Gln Ser Arg
             20                  25                  30

Ile Thr Pro Ile Gln Lys Pro Arg Gly Xaa Asp Pro Val Glu Ile Leu
         35                  40                  45

Gln Glu Arg Glu Tyr Arg Leu Gln Ala Arg Ile Ala His Arg Ile Gln
     50                  55                  60

Glu Leu Glu Asn Leu Pro Gly Ser Leu Ala Gly Asp Leu Arg Thr Lys
 65                  70                  75                  80

Ala Thr Ile Glu Leu Lys Ala Leu Arg Leu Leu Asn Phe Gln Arg Gln
                 85                  90                  95

Leu Arg Gln Glu Val Val Val Cys Met Arg Arg Asp Thr Ala Leu Glu
            100                 105                 110

Thr Ala Leu Asn Ala Lys Ala Tyr Lys Arg Xaa Ser Ala Ser Pro Cys
        115                 120                 125

Ala Arg Pro Ala Ser Leu Arg Ser Trp Arg Ser Ser Arg Arg Ser Ser
    130                 135                 140

Arg Ser Ala Ser Ala Gly Arg Ser Thr Arg Asn Thr Ser Ile Ala Phe
145                 150                 155                 160

Ser Ser Met Pro Arg Ile Ser Arg Asn Ile Thr Asp Pro Ser Gln Ala
                165                 170                 175

Lys Ser Arg Ser
            180
```

<210> 437

<211> 415
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (94)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (96)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (170)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 437
```
Arg Lys Tyr Leu Val Pro Leu Xaa Lys Lys Leu Tyr Leu Lys Trp Ala
  1               5                  10                  15

Leu Glu Glu Tyr Leu Asp Glu Phe Asp Pro Cys His Cys Arg Pro Cys
             20                  25                  30

Gln Asn Gly Gly Leu Ala Thr Val Glu Gly Thr His Cys Leu Cys His
         35                  40                  45

Cys Lys Pro Tyr Thr Phe Gly Ala Ala Cys Glu Gln Gly Val Leu Val
     50                  55                  60

Gly Asn Gln Ala Gly Gly Val Asp Gly Gly Trp Ser Cys Trp Ser Ser
 65                  70                  75                  80

Trp Ser Pro Cys Val Gln Gly Lys Lys Thr Arg Ser Arg Xaa Cys Xaa
                 85                  90                  95

Asn Pro Pro Pro Ser Gly Gly Gly Arg Ser Cys Val Gly Glu Thr Thr
            100                 105                 110

Glu Ser Thr Gln Cys Glu Asp Glu Glu Leu Glu His Leu Arg Leu Leu
        115                 120                 125

Glu Pro His Cys Phe Pro Leu Ser Leu Val Pro Thr Glu Phe Cys Pro
    130                 135                 140
```

Ser Pro Pro Ala Leu Lys Asp Gly Phe Val Gln Asp Glu Gly Thr Met
145 150 155 160

Phe Pro Val Gly Lys Asn Val Val Tyr Xaa Cys Asn Glu Gly Tyr Ser
165 170 175

Leu Ile Gly Asn Pro Val Ala Arg Cys Gly Glu Asp Leu Arg Trp Leu
180 185 190

Val Gly Glu Met His Cys Gln Lys Ile Ala Cys Val Leu Pro Val Leu
195 200 205

Met Asp Gly Ile Gln Ser His Pro Gln Lys Pro Phe Tyr Thr Val Gly
210 215 220

Glu Lys Val Thr Val Ser Cys Ser Gly Gly Met Ser Leu Glu Gly Pro
225 230 235 240

Ser Ala Phe Leu Cys Gly Ser Ser Leu Lys Trp Ser Pro Glu Met Lys
245 250 255

Asn Ala Arg Cys Val Gln Lys Glu Asn Pro Leu Thr Gln Ala Val Pro
260 265 270

Lys Cys Gln Arg Trp Glu Lys Leu Gln Asn Ser Arg Cys Val Cys Lys
275 280 285

Met Pro Tyr Glu Cys Gly Pro Ser Leu Asp Val Cys Ala Gln Asp Glu
290 295 300

Arg Ser Lys Arg Ile Leu Pro Leu Thr Val Cys Lys Met His Val Leu
305 310 315 320

His Cys Gln Gly Arg Asn Tyr Thr Leu Thr Gly Arg Asp Ser Cys Thr
325 330 335

Leu Pro Ala Ser Ala Glu Lys Ala Cys Gly Ala Cys Pro Leu Trp Gly
340 345 350

Lys Cys Asp Ala Glu Ser Ser Lys Cys Val Cys Arg Glu Ala Ser Glu
355 360 365

Cys Glu Glu Glu Gly Phe Ser Ile Cys Val Glu Val Asn Gly Lys Glu
370 375 380

Gln Thr Met Ser Glu Cys Glu Ala Gly Ala Leu Arg Cys Arg Gly Gln
385 390 395 400

Ser Ile Ser Val Thr Ser Ile Arg Pro Cys Ala Ala Glu Thr Gln
405 410 415

<210> 438
<211> 285
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (17)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 438
```
Leu Ile Arg Leu Thr Ile Gly Lys Ala Gly Ser Leu Gln Tyr Arg Xaa
  1               5                  10                  15

Xaa Xaa Phe Pro Gly Met Glu Ala Phe Leu Gly Ser Arg Ser Gly Leu
             20                  25                  30

Trp Ala Gly Gly Pro Ala Pro Gly Gln Phe Tyr Arg Ile Pro Ser Thr
         35                  40                  45

Pro Asp Ser Phe Met Asp Pro Ala Ser Ala Leu Tyr Arg Gly Pro Ile
     50                  55                  60

Thr Arg Thr Gln Asn Pro Met Val Thr Gly Thr Ser Val Leu Gly Val
 65                  70                  75                  80

Lys Phe Glu Gly Gly Val Val Ile Ala Ala Asp Met Leu Gly Ser Tyr
                 85                  90                  95

Gly Ser Leu Ala Arg Phe Arg Asn Ile Ser Arg Ile Met Arg Val Asn
            100                 105                 110

Asn Ser Thr Met Leu Gly Ala Ser Gly Asp Tyr Ala Asp Phe Gln Tyr
        115                 120                 125

Leu Lys Gln Val Leu Gly Gln Met Val Ile Asp Glu Glu Leu Leu Gly
    130                 135                 140
```

Asp Gly His Ser Tyr Ser Pro Arg Ala Ile His Ser Trp Leu Thr Arg
145 150 155 160

Ala Met Tyr Ser Arg Arg Ser Lys Met Asn Pro Leu Trp Asn Thr Met
165 170 175

Val Ile Gly Gly Tyr Ala Asp Gly Glu Ser Phe Leu Gly Tyr Val Asp
180 185 190

Met Leu Gly Val Ala Tyr Glu Ala Pro Ser Leu Ala Thr Gly Tyr Gly
195 200 205

Ala Tyr Leu Ala Gln Pro Leu Leu Arg Glu Val Leu Glu Lys Gln Pro
210 215 220

Val Leu Ser Gln Thr Glu Ala Arg Asp Leu Val Glu Arg Cys Met Arg
225 230 235 240

Val Leu Tyr Tyr Arg Asp Ala Arg Ser Tyr Asn Arg Phe Gln Ile Ala
245 250 255

Thr Val Thr Glu Lys Gly Val Glu Ile Glu Gly Pro Leu Ser Thr Glu
260 265 270

Thr Asn Trp Asp Ile Ala His Met Ile Ser Gly Phe Glu
275 280 285

<210> 439
<211> 185
<212> PRT
<213> Homo sapiens

<400> 439
Asn Ser Ala Ala His Lys Lys Gly Lys Leu Pro Ile Val Asn Glu Asp
1 5 10 15

Asp Glu Leu Val Ala Ile Ile Ala Arg Thr Asp Leu Lys Lys Asn Arg
20 25 30

Asp Tyr Pro Leu Ala Ser Lys Asp Ala Lys Lys Gln Leu Leu Cys Gly
35 40 45

Ala Ala Ile Gly Thr His Glu Asp Asp Lys Tyr Arg Leu Asp Leu Leu
50 55 60

Ala Gln Ala Gly Val Asp Val Val Val Leu Asp Ser Ser Gln Gly Asn
65 70 75 80

Ser Ile Phe Gln Ile Asn Met Ile Lys Tyr Ile Lys Asp Lys Tyr Pro

```
                85                  90                  95

Asn Leu Gln Val Ile Gly Gly Asn Val Val Thr Ala Ala Gln Ala Lys
            100                 105                 110

Asn Leu Ile Asp Ala Gly Val Asp Ala Leu Arg Val Gly Met Gly Ser
        115                 120                 125

Gly Ser Ile Cys Ile Thr Gln Glu Val Leu Ala Cys Gly Arg Pro Gln
    130                 135                 140

Ala Thr Ala Val Tyr Lys Val Ser Glu Tyr Ala Arg Arg Phe Gly Val
145                 150                 155                 160

Pro Val Ile Ala Asp Gly Gly Ile Gln Asn Val Gly His Ile Ala Lys
                165                 170                 175

Ala Leu Ala Leu Gly Ala Pro Gln Ser
            180                 185



<210> 440
<211> 211
<212> PRT
<213> Homo sapiens

<400> 440
Leu Gln Gly Arg Ser Thr Pro Ile Trp Pro Ala Leu Ala Thr Val Thr
  1               5                  10                  15

Ser Arg Thr Pro Ala Leu Gly Pro Gln Ala Gly Ile Asp Thr Asn Glu
            20                  25                  30

Ile Ala Pro Leu Glu Pro Asp Ala Pro Pro Asp Ala Cys Glu Ala Ser
        35                  40                  45

Phe Asp Ala Val Ser Thr Ile Arg Gly Glu Leu Phe Phe Phe Lys Ala
    50                  55                  60

Gly Phe Val Trp Arg Leu Arg Gly Gly Gln Leu Gln Pro Gly Tyr Pro
65                  70                  75                  80

Ala Leu Ala Ser Arg His Trp Gln Gly Leu Pro Ser Pro Val Asp Ala
                85                  90                  95

Ala Phe Glu Asp Ala Gln Gly His Ile Trp Phe Phe Gln Gly Ala Gln
            100                 105                 110

Tyr Trp Val Tyr Asp Gly Glu Lys Pro Val Leu Gly Pro Ala Pro Leu
        115                 120                 125
```

```
Thr Glu Leu Gly Leu Val Arg Phe Pro Val His Ala Ala Leu Val Trp
    130                 135                 140

Gly Pro Glu Lys Asn Lys Ile Tyr Phe Phe Arg Gly Arg Asp Tyr Trp
145                 150                 155                 160

Arg Phe His Pro Ser Thr Arg Arg Val Asp Ser Pro Val Pro Arg Arg
                165                 170                 175

Pro Leu Thr Gly Glu Gly Cys Pro Leu Arg Ser Thr Leu Pro Ser Arg
            180                 185                 190

Met Leu Met Ala Met Pro Thr Ser Cys Ala Ala Ala Ser Thr Gly Ser
        195                 200                 205

Leu Thr Leu
    210
```

```
<210> 441
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (40)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 441
Gly Gly Ala Gly Lys Leu Leu Ser Phe Thr His Ser Ala Pro Trp Ser
  1               5                  10                  15

Arg Leu Trp Ser Ser Leu Gly Lys Arg Val Thr Gly Glu Ser Gln Gly
            20                  25                  30

Leu Glu Lys Leu Pro Gly Thr Xaa Asp Gly Leu Ala Ala Leu Thr Gln
        35                  40                  45

Asp Pro Leu Pro Leu Pro Pro Pro Leu Cys Arg Asn Thr Gly Thr Pro
    50                  55                  60

Arg Gly Lys Met Ser Phe Ser Arg Leu Gln Phe Ser Pro Arg Lys Leu
65                  70                  75                  80
```

<210> 442
<211> 567
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (205)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (212)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (469)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (503)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (505)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (517)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (535)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (546)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 442
Asn Val His Leu Tyr Ile Met Tyr Tyr Met Glu Ala Lys His Ala Val
1 5 10 15

Ser Phe Met Thr Cys Thr Gln Asn Val Ala Pro Asp Met Phe Arg Thr

20 25 30

Ile Pro Pro Glu Ala Asn Ile Pro Ile Pro Val Lys Ser Asp Met Val
35 40 45

Met Met His Glu His His Lys Glu Thr Glu Tyr Lys Asp Lys Ile Pro
50 55 60

Leu Leu Gln Gln Pro Lys Arg Glu Glu Glu Glu Val Leu Asp Gln Gly
65 70 75 80

Asp Phe Tyr Ser Leu Leu Ser Lys Leu Leu Gly Glu Arg Glu Asp Val
85 90 95

Val His Val His Lys Tyr Asn Pro Thr Glu Lys Ala Glu Ser Glu Ser
100 105 110

Asp Leu Val Ala Glu Ile Ala Asn Val Val Gln Lys Lys Asp Leu Gly
115 120 125

Arg Ser Asp Ala Arg Glu Gly Ala Glu His Glu Arg Gly Asn Ala Ile
130 135 140

Leu Val Arg Asp Arg Ile His Lys Phe His Arg Leu Val Ser Thr Leu
145 150 155 160

Arg Pro Pro Glu Ser Arg Val Phe Ser Leu Gln Gln Pro Pro Pro Gly
165 170 175

Glu Gly Thr Trp Glu Pro Glu His Thr Gly Asp Phe His Met Glu Glu
180 185 190

Ala Leu Asp Trp Pro Gly Val Tyr Leu Leu Pro Gly Xaa Val Ser Gly
195 200 205

Val Ala Leu Xaa Pro Lys Asn Asn Leu Val Ile Phe His Arg Gly Asp
210 215 220

His Val Trp Asp Gly Asn Ser Phe Asp Ser Lys Phe Val Tyr Gln Gln
225 230 235 240

Ile Gly Leu Gly Pro Ile Glu Glu Asp Thr Ile Leu Val Ile Asp Pro
245 250 255

Asn Asn Ala Ala Val Leu Gln Ser Ser Gly Lys Asn Leu Phe Tyr Leu
260 265 270

Pro His Gly Leu Ser Ile Asp Lys Asp Gly Asn Tyr Trp Val Thr Asp
275 280 285

Val Ala Leu His Gln Val Phe Lys Leu Asp Pro Asn Asn Lys Glu Gly

```
    290                 295                 300

Pro Val Leu Ile Leu Gly Arg Ser Met Gln Pro Gly Ser Asp Gln Asn
305                 310                 315                 320

His Phe Cys Gln Pro Thr Asp Val Ala Val Asp Pro Gly Thr Gly Ala
                325                 330                 335

Ile Tyr Val Ser Asp Gly Tyr Cys Asn Ser Arg Ile Val Gln Phe Ser
            340                 345                 350

Pro Ser Gly Lys Phe Ile Thr Gln Trp Gly Glu Glu Ser Ser Gly Ser
        355                 360                 365

Ser Pro Leu Pro Gly Gln Phe Thr Val Pro His Ser Leu Ala Leu Val
    370                 375                 380

Pro Leu Leu Gly Gln Leu Cys Val Ala Asp Arg Glu Asn Gly Arg Ile
385                 390                 395                 400

Gln Cys Phe Lys Thr Asp Thr Lys Glu Phe Val Arg Glu Ile Lys His
                405                 410                 415

Ser Ser Phe Gly Arg Asn Val Phe Ala Ile Ser Tyr Ile Pro Gly Leu
            420                 425                 430

Leu Phe Ala Val Asn Gly Lys Pro His Phe Gly Asp Gln Glu Pro Val
        435                 440                 445

Gln Gly Phe Val Met Asn Phe Ser Asn Gly Glu Ile Ile Asp Ile Phe
    450                 455                 460

Lys Pro Val Arg Xaa Leu Leu Asp Met Pro His Asp Ile Val Ala Ser
465                 470                 475                 480

Glu Asp Gly Thr Val Tyr Ile Gly Arg Cys Ser Tyr Gln His Arg Val
                485                 490                 495

Gly Ser Ser Thr Leu Asp Xaa Arg Xaa Leu Gly Thr Ser Val Gln Phe
            500                 505                 510

Lys Lys Gly Leu Xaa Ile Glu Val Gln Gly Asn Pro Lys Lys Pro Glu
        515                 520                 525

Gly Ile Cys Cys Phe Pro Xaa Thr Thr Leu Arg Val Ile Pro Val Val
    530                 535                 540

Gly Xaa Trp Arg Gly His Gly Pro Asn Leu Ile Pro Val Gly Lys Asn
545                 550                 555                 560

Pro Arg Gly Pro Leu Gly Arg
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565

<210> 443
<211> 129
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (123)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (127)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (129)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 443
Arg Pro Ser Cys Ser Pro Gly Ser Val Ser Ala Ala Ala Val Asn Met
1 5 10 15

Glu Pro Pro Asp Ala Pro Ala Gln Ala Arg Gly Ala Pro Arg Leu Leu
20 25 30

Leu Leu Ala Val Leu Leu Ala Ala His Pro Asp Ala Gln Ala Glu Val
35 40 45

Arg Leu Ser Val Pro Pro Leu Val Glu Val Met Arg Gly Lys Ser Val
50 55 60

Ile Leu Asp Cys Thr Pro Thr Gly Thr His Asp His Tyr Met Leu Glu
65 70 75 80

Trp Phe Leu Thr Asp Arg Ser Gly Ala Arg Pro Arg Leu Ala Ser Ala
85 90 95

Glu Met Gln Gly Ser Glu Leu Gln Val Thr Met His Asp Thr Arg Gly
100 105 110

Arg Ser Pro Pro Tyr Gln Leu Gly Leu Pro Xaa Gly Ala Trp Xaa Leu
115 120 125

Xaa

<210> 444
<211> 131
<212> PRT
<213> Homo sapiens

<400> 444
Glu Pro Arg Val Glu Arg Glu Thr Pro Gly Gln Pro Phe Ser Ser Ser
1   5   10   15

Phe Pro Ser Pro Ser Pro Phe Pro Asn Val Ala Ser Met Trp Val Leu
            20   25   30

Gly Thr Trp Glu Lys Pro Leu Leu Cys His Phe Phe Ser Leu Phe Pro
        35   40   45

Ser Ser Pro Pro Thr Val Trp Leu Met Met Ser Ser Gly Val Met Val
    50   55   60

Thr Thr Pro Cys Ser Leu Phe Trp Tyr Phe Pro Cys Gln Phe Pro Leu
65   70   75   80

Ser Ala Arg Leu Cys Pro Lys Ile Pro Ser Ala Ser Ser Leu His Val
                85   90   95

Ala Glu Gly Pro Gly Leu Pro Gln Val Pro Cys Leu Ser Asn Lys Val
            100   105   110

Glu Thr Ile Lys Pro Gly Lys Lys Lys Lys Gly Gly Arg Ser Lys Gly
        115   120   125

Ser Pro Arg
    130

<210> 445
<211> 405
<212> PRT
<213> Homo sapiens

<400> 445
Gly Thr Gly Leu Val Pro Ile Arg Gln Ser Thr Lys Phe Asp Ser Ser
1   5   10   15

Leu Asp Arg Lys Asp Lys Phe Ser Phe Asp Leu Gly Lys Gly Glu Val
            20   25   30

Ile Lys Ala Trp Asp Ile Ala Ile Ala Thr Met Lys Val Gly Glu Val

35 40 45

Cys His Ile Thr Cys Lys Pro Glu Tyr Ala Tyr Gly Ser Ala Gly Ser
50 55 60

Pro Pro Lys Ile Pro Pro Asn Ala Thr Leu Val Phe Glu Val Glu Leu
65 70 75 80

Phe Glu Phe Lys Gly Glu Asp Leu Thr Glu Glu Glu Asp Gly Gly Ile
85 90 95

Ile Arg Arg Ile Gln Thr Arg Gly Glu Gly Tyr Ala Lys Pro Asn Glu
100 105 110

Gly Ala Ile Val Glu Val Ala Leu Glu Gly Tyr Tyr Lys Asp Lys Leu
115 120 125

Phe Asp Gln Arg Glu Leu Arg Phe Glu Ile Gly Glu Gly Glu Asn Leu
130 135 140

Asp Leu Pro Tyr Gly Leu Glu Arg Ala Ile Gln Arg Met Glu Lys Gly
145 150 155 160

Glu His Ser Ile Val Tyr Leu Lys Pro Ser Tyr Ala Phe Gly Ser Val
165 170 175

Gly Lys Glu Lys Phe Gln Ile Pro Pro Asn Ala Glu Leu Lys Tyr Glu
180 185 190

Leu His Leu Lys Ser Phe Glu Lys Ala Lys Glu Ser Trp Glu Met Asn
195 200 205

Ser Glu Glu Lys Leu Glu Gln Ser Thr Ile Val Lys Glu Arg Gly Thr
210 215 220

Val Tyr Phe Lys Glu Gly Lys Tyr Lys Gln Ala Leu Leu Gln Tyr Lys
225 230 235 240

Lys Ile Val Ser Trp Leu Glu Tyr Glu Ser Ser Phe Ser Asn Glu Glu
245 250 255

Ala Gln Lys Ala Gln Ala Leu Arg Leu Ala Ser His Leu Asn Leu Ala
260 265 270

Met Cys His Leu Lys Leu Gln Ala Phe Ser Ala Ala Ile Glu Ser Cys
275 280 285

Asn Lys Ala Leu Glu Leu Asp Ser Asn Asn Glu Lys Gly Leu Phe Arg
290 295 300

Arg Gly Glu Ala His Leu Ala Val Asn Asp Phe Glu Leu Ala Arg Ala

305 310 315 320

Asp Phe Gln Lys Val Leu Gln Leu Tyr Pro Asn Asn Lys Ala Ala Lys
325 330 335

Thr Gln Leu Ala Val Cys Gln Gln Arg Ile Arg Arg Gln Leu Ala Arg
340 345 350

Glu Lys Lys Leu Tyr Ala Asn Met Phe Glu Arg Leu Ala Glu Glu Glu
355 360 365

Asn Lys Ala Lys Ala Glu Ala Ser Ser Gly Asp His Pro Thr Asp Thr
370 375 380

Glu Met Lys Glu Glu Gln Lys Ser Asn Thr Ala Gly Ser Gln Ser Gln
385 390 395 400

Val Glu Thr Glu Ala
405

<210> 446
<211> 232
<212> PRT
<213> Homo sapiens

<400> 446
Pro Leu Val Pro Ser Ser Gln Lys Ala Leu Leu Leu Glu Leu Lys Gly
1 5 10 15

Leu Gln Glu Glu Pro Val Glu Gly Phe Arg Val Thr Leu Val Asp Glu
20 25 30

Gly Asp Leu Tyr Asn Trp Glu Val Ala Ile Phe Gly Pro Pro Asn Thr
35 40 45

Tyr Tyr Glu Gly Gly Tyr Phe Lys Ala Arg Leu Lys Phe Pro Ile Asp
50 55 60

Tyr Pro Tyr Ser Pro Pro Ala Phe Arg Phe Leu Thr Lys Met Trp His
65 70 75 80

Pro Asn Ile Tyr Glu Thr Gly Asp Val Cys Ile Ser Ile Leu His Pro
85 90 95

Pro Val Asp Asp Pro Gln Ser Gly Glu Leu Pro Ser Glu Arg Trp Asn
100 105 110

Pro Thr Gln Asn Val Arg Thr Ile Leu Leu Ser Val Ile Ser Leu Leu
115 120 125

Asn Glu Pro Asn Thr Phe Ser Pro Ala Asn Val Asp Ala Ser Val Met
    130   135   140

Tyr Arg Lys Trp Lys Glu Ser Lys Gly Lys Asp Arg Glu Tyr Thr Asp
145   150   155   160

Ile Ile Arg Lys Gln Val Leu Gly Thr Arg Trp Thr Arg Val Asn Gly
                165   170   175

Val Lys Val Pro Thr Thr Leu Ala Glu Tyr Cys Val Lys Thr Lys Ala
            180   185   190

Pro Ala Pro Asp Glu Gly Ser Asp Leu Phe Tyr Asp Asp Tyr Tyr Glu
        195   200   205

Asp Gly Glu Val Glu Glu Glu Ala Asp Ser Cys Phe Gly Asp Asp Glu
    210   215   220

Asp Asp Ser Gly Thr Glu Glu Ser
225   230

<210> 447
<211> 356
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (53)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (191)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (263)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 447
Cys Ser Pro Pro Pro Pro Pro Ala Ala Ala Ala Xaa Ala Ala Ala Ala

```
1               5                   10                  15

Ala Met Ala Gln Tyr Lys Gly Ala Ala Ser Glu Ala Gly Arg Ala Met
            20                  25                  30

His Leu Met Lys Lys Arg Glu Lys Gln Arg Glu Gln Met Glu Gln Met
        35                  40                  45

Lys Gln Arg Ile Xaa Glu Glu Asn Ile Met Lys Ser Asn Ile Asp Lys
    50                  55                  60

Lys Phe Ser Ala His Tyr Asp Ala Val Glu Ala Glu Leu Lys Ser Ser
65                  70                  75                  80

Thr Val Gly Leu Val Thr Leu Asn Asp Met Lys Ala Lys Gln Glu Ala
                85                  90                  95

Leu Val Lys Glu Arg Glu Lys Gln Leu Ala Lys Lys Glu Gln Ser Lys
            100                 105                 110

Glu Leu Gln Met Lys Leu Glu Lys Leu Arg Glu Lys Glu Arg Lys Lys
        115                 120                 125

Glu Ala Lys Arg Lys Ile Ser Ser Leu Ser Phe Thr Leu Glu Glu Glu
    130                 135                 140

Glu Glu Gly Gly Glu Glu Glu Glu Glu Ala Ala Met Tyr Glu Glu Glu
145                 150                 155                 160

Met Glu Arg Glu Glu Ile Thr Thr Lys Lys Arg Lys Leu Gly Lys Asn
                165                 170                 175

Pro Asp Val Asp Thr Ser Phe Leu Pro Asp Arg Asp Arg Glu Xaa Glu
            180                 185                 190

Glu Asn Arg Leu Arg Glu Glu Leu Arg Gln Glu Trp Glu Ala Lys Gln
        195                 200                 205

Glu Lys Ile Lys Ser Glu Glu Ile Glu Ile Thr Phe Ser Tyr Trp Asp
    210                 215                 220

Gly Ser Gly His Arg Arg Thr Val Lys Met Arg Lys Gly Asn Thr Met
225                 230                 235                 240

Gln Gln Phe Leu Gln Lys Ala Leu Glu Ile Leu Arg Lys Asp Phe Ser
                245                 250                 255

Glu Leu Arg Ser Ala Gly Xaa Glu Gln Leu Met Tyr Ile Lys Glu Asp
            260                 265                 270

Leu Ile Ile Pro His His His Ser Phe Tyr Asp Phe Ile Val Thr Lys
```

275 280 285

Ala Arg Gly Lys Ser Gly Pro Leu Phe Asn Phe Asp Val His Asp Asp
290 295 300

Val Arg Leu Leu Ser Asp Ala Thr Val Glu Lys Asp Glu Ser His Ala
305 310 315 320

Gly Lys Val Val Leu Arg Ser Trp Tyr Glu Lys Asn Lys His Ile Phe
325 330 335

Pro Ala Ser Arg Trp Glu Pro Tyr Asp Pro Glu Lys Lys Trp Asp Lys
340 345 350

Tyr Thr Ile Arg
355

<210> 448
<211> 88
<212> PRT
<213> Homo sapiens

<400> 448
Lys Thr His Lys Met Cys Asp Ala Phe Val Gly Thr Trp Lys Leu Val
1 5 10 15

Ser Ser Glu Asn Phe Asp Asp Tyr Met Lys Glu Val Gly Val Gly Phe
20 25 30

Ala Thr Arg Lys Val Ala Gly Met Ala Lys Pro Asn Met Ile Ile Ser
35 40 45

Val Asn Gly Asp Val Ile Thr Ile Lys Ser Glu Ser Thr Phe Lys Asn
50 55 60

Thr Glu Ile Ser Phe Ile Leu Gly Gln Glu Phe Asp Glu Ala Leu Gln
65 70 75 80

Met Thr Gly Lys Ser Arg Ala Pro
85

<210> 449
<211> 171
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (72)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (132)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 449
Leu Ile Leu Val Leu Met Phe Val Val Trp Met Lys Arg Arg Asp Lys
1 5 10 15

Glu Arg Gln Ala Lys Gln Leu Leu Ile Asp Pro Glu Asp Asp Val Arg
20 25 30

Asp Asn Ile Leu Lys Tyr Asp Glu Glu Gly Gly Gly Glu Glu Asp Gln
35 40 45

Asp Tyr Asp Leu Ser Gln Leu Gln Gln Pro Asp Thr Val Glu Pro Asp
50 55 60

Ala Ile Lys Pro Val Gly Ile Xaa Arg Met Asp Glu Arg Pro Ile His
65 70 75 80

Ala Glu Pro Gln Tyr Pro Val Arg Ser Ala Ala Pro His Pro Gly Asp
85 90 95

Ile Gly Asp Phe Ile Asn Glu Gly Leu Lys Ala Ala Asp Asn Asp Pro
100 105 110

Thr Ala Pro Pro Tyr Asp Ser Leu Leu Val Phe Asp Tyr Glu Gly Ser
115 120 125

Gly Ser Thr Xaa Gly Ser Leu Ser Ser Leu Asn Ser Ser Ser Ser Gly
130 135 140

Gly Glu Gln Asp Tyr Asp Tyr Leu Asn Asp Trp Gly Pro Arg Phe Lys
145 150 155 160

Lys Leu Ala Asp Met Tyr Gly Gly Gly Asp Asp
165 170

<210> 450
<211> 34
<212> PRT
<213> Homo sapiens

<400> 450

Lys Val Lys Ala Cys Cys Lys Asp Ile Phe Phe Leu Leu Leu Glu Gly
1 5 10 15

Asn Thr Lys Arg Lys Ile Ser Phe Phe His Gly Ala Phe Asp Asn Phe
20 25 30

Ser Leu

<210> 451
<211> 148
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (43)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (89)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 451
Arg Thr Leu His Pro Ala Thr Gly Pro Arg Ala Arg Pro Pro Arg Gly
1 5 10 15

Trp Arg Arg Arg Leu Cys Ala Gln Gly Pro Ala Pro Asp Trp Asp Pro
20 25 30

Gly Val Pro Pro Gly Leu Ala Ser Cys Gly Xaa Thr Val Trp Leu His
35 40 45

Phe Ser Asp Pro Ser Leu Gly Arg Lys Val Lys Glu Thr Gly Pro Ala
50 55 60

Ser Ala Phe Gly Leu Trp Phe Leu Asp Arg Val Leu Ser Pro Ser Pro
65 70 75 80

Pro Ser Ser Pro Asn Leu Ser His Xaa Arg Pro Leu Pro Ala Ala Pro
85 90 95

Ser Leu Leu Gly Ile Gly Ser Pro Glu Pro Pro Ser Pro Glu Pro Pro
100 105 110

Thr Pro Leu Pro Gly Pro Cys Gly Cys Trp Ala Ser His Leu Lys Glu
115 120 125

Gly Lys Val Val Gln Pro Glu Pro Val Glu Gln Cys Pro Val Trp Pro
    130   135   140

Pro Lys Pro Lys
145

<210> 452
<211> 83
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (19)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (28)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (64)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (77)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (79)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 452
Asp Ser His Arg Pro Arg Ala Met Arg Ala Leu Trp Val Leu Gly Leu
  1   5   10   15

Ser Cys Xaa Leu Leu Thr Phe Gly Ser Val Arg Xaa Asp Asp Glu Val
             20   25   30

Asp Val Asp Gly Thr Val Glu Glu Asp Leu Gly Lys Ser Arg Glu Gly
         35   40   45

Ser Arg Thr Asp Asp Glu Val Val Gln Arg Glu Glu Glu Ala Ile Xaa
     50   55   60

Val Gly Trp Ile Lys Cys Ile Pro Asn Lys Arg Thr Xaa Glu Xaa Lys
65 70 75 80

Ser Arg Lys

<210> 453
<211> 240
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (234)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 453
Gly Trp Leu Pro Cys Gly Ser Ser Val Val Pro Ala Thr Pro Gly Ser
1 5 10 15

Pro Pro Ser Arg Phe Trp Leu Leu Pro Ala Met Ala Leu Arg Val Leu
20 25 30

Leu Leu Thr Ala Leu Thr Leu Cys His Gly Phe Asn Leu Asp Thr Glu
35 40 45

Asn Ala Met Thr Phe Gln Glu Asn Ala Arg Gly Phe Gly Gln Ser Val
50 55 60

Val Gln Leu Gln Gly Ser Arg Val Val Val Gly Ala Pro Gln Glu Ile
65 70 75 80

Val Ala Ala Asn Gln Arg Gly Ser Leu Tyr Gln Cys Asp Tyr Ser Thr
85 90 95

Gly Ser Cys Glu Pro Ile His Leu Gln Val Pro Val Glu Ala Val Asn
100 105 110

Met Ser Leu Gly Leu Ser Leu Ala Ala Thr Thr Ser Pro Pro Gln Leu
115 120 125

Leu Ala Cys Gly Pro Thr Val His Gln Thr Cys Ser Glu Asn Thr Tyr
130 135 140

Val Lys Gly Leu Cys Phe Leu Phe Gly Ser Asn Leu Arg Gln Gln Pro
145 150 155 160

Gln Lys Phe Pro Glu Ala Leu Arg Gly Cys Pro Gln Glu Asp Ser Asp
165 170 175

Ile Ala Phe Leu Ile Asp Gly Ser Gly Ser Ile Ile Pro His Asp Phe
180 185 190

Arg Arg Met Lys Glu Phe Val Ser Thr Val Met Glu Gln Leu Lys Lys
195 200 205

Ser Lys Thr Leu Phe Ser Leu Met Gln Tyr Ser Glu Glu Phe Arg Ile
210 215 220

His Phe Thr Ser Lys Ser Ser Arg Thr Xaa Leu Thr Gln Asp His Trp
225 230 235 240

<210> 454
<211> 244
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (206)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (227)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (229)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (239)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 454
Lys Trp Cys Ser Trp Thr Leu Leu Lys Ile Trp Glu Val Thr Cys Thr
1 5 10 15

Trp Lys Leu Pro Thr Leu Ala Lys Phe Ser Pro Tyr Leu Gly Gln Met
20 25 30

Ile Asn Leu Arg Arg Leu Leu Leu Ser His Ile His Ala Ser Ser Tyr

35 40 45

Ile Ser Pro Glu Lys Glu Glu Gln Tyr Ile Ala Gln Phe Thr Ser Gln
50 55 60

Phe Leu Ser Leu Gln Cys Leu Gln Leu Leu Tyr Val Asp Ser Leu Phe
65 70 75 80

Phe Leu Arg Gly Arg Leu Asp Gln Leu Leu Arg His Val Met Asn Pro
85 90 95

Leu Glu Thr Leu Ser Ile Thr Asn Cys Arg Leu Ser Glu Gly Asp Val
100 105 110

Met His Leu Ser Gln Ser Pro Ser Val Ser Gln Leu Ser Val Leu Ser
115 120 125

Leu Ser Gly Val Met Leu Thr Asp Val Ser Pro Glu Pro Leu Gln Ala
130 135 140

Leu Leu Glu Arg Ala Ser Ala Thr Leu Gln Asp Leu Val Phe Asp Glu
145 150 155 160

Cys Gly Ile Thr Asp Asp Gln Leu Leu Ala Leu Leu Pro Ser Leu Ser
165 170 175

His Cys Ser Gln Leu Thr Thr Leu Ser Phe Tyr Gly Asn Ser Ile Ser
180 185 190

Ile Ser Ala Leu Gln Ser Leu Leu Gln His Leu Ile Gly Xaa Ser Asn
195 200 205

Leu Thr His Val Leu Tyr Pro Val Pro Leu Glu Ser Tyr Glu Asp Ile
210 215 220

His Gly Xaa Leu Xaa Leu Glu Arg Leu Leu Ser Ala Cys Gln Xaa Gln
225 230 235 240

Gly Val Ala Val

<210> 455
<211> 195
<212> PRT
<213> Homo sapiens

<400> 455
His Glu Gly Thr Gln Ser Phe Val Phe Gln Arg Glu Glu Ile Ala Gln
1 5 10 15

Leu Ala Arg Gln Tyr Ala Gly Leu Asp His Glu Leu Ala Phe Ser Arg
20 25 30

Leu Ile Val Glu Leu Arg Arg Leu His Pro Gly His Val Leu Pro Asp
35 40 45

Glu Glu Leu Gln Trp Val Phe Val Asn Ala Gly Gly Trp Met Gly Ala
50 55 60

Met Cys Leu Leu His Ala Ser Leu Ser Glu Tyr Val Leu Leu Phe Gly
65 70 75 80

Thr Ala Leu Gly Ser Arg Gly His Ser Gly Arg Tyr Trp Ala Glu Ile
85 90 95

Ser Asp Thr Ile Ile Ser Gly Thr Phe His Gln Trp Arg Glu Gly Thr
100 105 110

Thr Lys Ser Glu Val Phe Tyr Pro Gly Glu Thr Val Val His Gly Pro
115 120 125

Gly Glu Ala Thr Ala Val Glu Trp Gly Pro Asn Thr Trp Met Val Glu
130 135 140

Tyr Gly Arg Gly Val Ile Pro Ser Thr Leu Ala Phe Ala Leu Ala Asp
145 150 155 160

Thr Val Phe Ser Thr Gln Asp Phe Leu Thr Leu Phe Tyr Thr Leu Arg
165 170 175

Ser Tyr Ala Arg Gly Leu Arg Leu Glu Leu Thr Thr Tyr Leu Phe Gly
180 185 190

Gln Asp Pro
195

<210> 456
<211> 36
<212> PRT
<213> Homo sapiens

<400> 456
Leu Val Thr Leu Leu His Ala Met Gln Ala Arg Asp Lys Thr Leu Gly
1 5 10 15

Leu Ala Thr Leu Cys Ile Gly Gly Gly Gln Gly Ile Ala Met Val Ile
20 25 30

```
Glu Arg Leu Asn
        35



<210> 457
<211> 152
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (86)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (114)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 457
Val Thr Ala Ala Ala Ser Val Arg Ala Leu Gln Val Thr Val Ala Gly
  1               5                  10                  15

Leu Leu Leu Val Phe Phe Leu Phe Gly Ala Pro Leu Asp Ser Leu Pro
             20                  25                  30

Ser Met Lys Ala Leu Ser Pro Val Arg Gly Cys Tyr Glu Ala Val Cys
         35                  40                  45

Cys Leu Ser Glu Arg Ser Leu Ala Ile Ala Arg Gly Arg Gly Lys Gly
     50                  55                  60

Pro Ala Ala Glu Glu Pro Leu Ser Leu Leu Asp Asp Met Asn His Cys
 65                  70                  75                  80

Tyr Ser Arg Leu Arg Xaa Leu Val Pro Gly Val Pro Arg Gly Thr Gln
                 85                  90                  95

Leu Ser Gln Val Glu Ile Leu Gln Arg Val Ile Asp Tyr Ile Leu Asp
            100                 105                 110

Leu Xaa Val Val Leu Ala Glu Pro Ala Pro Gly Pro Pro Asp Gly Pro
        115                 120                 125

His Leu Pro Ile Gln Thr Ala Glu Leu Ala Pro Glu Leu Val Ile Ser
    130                 135                 140

Asn Asp Lys Arg Ser Phe Cys His
145                 150
```

<210> 458
<211> 31
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (17)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 458
Leu Leu Asn Asn Phe Ile Phe Leu Glu Thr His Tyr Leu Trp Ala Cys
1 5 10 15

Xaa Thr Trp Thr Ile Trp Pro Asn Xaa Leu Asp Lys Lys Gly Xaa
20 25 30

<210> 459
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (28)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (72)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (130)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 459
Asp Pro Arg Val Arg Glu Thr Thr Val Lys Ala Arg Ala Arg Ser Gln
1   5   10   15

His Ala Gly Gly Pro Glu Leu Gly Leu Ser Gln Xaa Tyr Val Thr Pro
            20   25   30

Arg Arg Pro Phe Glu Lys Ser Arg Leu Asp Gln Glu Leu Lys Leu Ile
        35   40   45

Gly Glu Tyr Gly Leu Arg Asn Lys Arg Glu Val Trp Arg Val Lys Phe
    50   55   60

Thr Leu Ala Lys Ile Arg Lys Xaa Ala Arg Glu Leu Leu Thr Leu Asp
65   70   75   80

Glu Lys Asp Pro Arg Arg Leu Phe Glu Gly Asn Ala Leu Leu Arg Arg
                85   90   95

Leu Val Arg Ile Gly Val Leu Asp Glu Gly Lys Met Lys Leu Asp Tyr
            100   105   110

Ile Leu Gly Leu Lys Met Arg Ile Leu Gly Glu Xaa Ser Ala Asp Pro
        115   120   125

Gly Xaa Ser Ser Trp Gly Trp Pro Ile His Pro Pro Cys Pro Val Leu
    130   135   140

Ile Arg Gln Ala Thr Gln Val Arg Lys Gln Val Val Asn
145   150   155

<210> 460
<211> 136
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (119)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (130)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 460
Ile Trp Ala Pro Phe Pro His His Gln Gly Ser Gly Ser Gln Val Ser
1   5   10   15

Ser Tyr Gly Thr Gly Ala Leu Lys Ser His Ile Met Ala Ala Lys Ala
            20   25   30

Val Ala Asn Thr Met Arg Thr Ser Leu Gly Pro Asn Gly Leu Asp Lys
        35   40   45

Met Met Val Asp Lys Asp Gly Asp Val Thr Val Thr Asn Asp Gly Ala
    50   55   60

Thr Ile Leu Ser Met Met Asp Val Asp His Gln Ile Ala Lys Leu Met
65   70   75   80

Val Glu Leu Ser Lys Ser Gln Asp Asp Glu Ile Gly Asp Gly Asp His
                85   90   95

Gly Gly Gly Cys Pro Gly Arg Arg Pro Ala Gly Arg Arg Pro Ser Ser
            100   105   110

Cys Trp Thr Ala Ala Phe Xaa Arg Ser Gly Ser Pro Thr Val Thr Ser
        115   120   125

Arg Xaa Pro Ala Leu Ala Xaa Glu
    130   135

<210> 461
<211> 390
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (11)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (14)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (375)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (382)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (383)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (386)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (387)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 461
Cys Gly Asn Trp Trp Val Pro Arg Ala Gly Xaa Asn Trp Xaa Arg Gly
1 5 10 15

Ser Arg Phe Leu Phe Val Asp Arg Cys Asp Arg His Leu Thr Met Gln
20 25 30

Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu
35 40 45

Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu
50 55 60

Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu
65 70 75 80

Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr
85 90 95

Leu His Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys
100 105 110

Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr
115 120 125

Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro
    130   135   140

Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg
145   150   155   160

Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val
                165   170   175

Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu Thr Gly
            180   185   190

Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val
        195   200   205

Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg
    210   215   220

Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp
225   230   235   240

Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg
                245   250   255

Gly Gly Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr
            260   265   270

Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile
        275   280   285

Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala
    290   295   300

Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln
305   310   315   320

Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Met Gln
                325   330   335

Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu
            340   345   350

Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Arg Ser Arg Gln Gly Arg
        355   360   365

His Pro Pro Asp Gln Gln Xaa Leu Ile Leu Leu Gly Lys Xaa Xaa Lys
    370   375   380

Trp Xaa Xaa Pro Phe Asp
385   390

<210> 462
<211> 171
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (74)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (142)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (155)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 462
```
Cys Ser Thr Val Arg Ile Pro Gly Ser Thr His Ala Ser Gly Leu Ser
  1               5                  10                  15

Arg Arg Ala Ser Pro Val Tyr Leu Ala Ser Met Ser Gly Arg Gly Lys
             20                  25                  30

Thr Gly Gly Lys Ala Arg Ala Lys Ala Lys Ser Arg Ser Ser Arg Ala
         35                  40                  45

Gly Leu Gln Phe Pro Val Gly Arg Val His Arg Leu Leu Arg Lys Gly
     50                  55                  60

His Tyr Ala Glu Arg Val Gly Ala Gly Xaa Pro Val Tyr Leu Ala Ala
 65                  70                  75                  80

Val Leu Glu Tyr Leu Thr Ala Glu Ile Leu Glu Leu Ala Gly Asn Ala
                 85                  90                  95

Ala Arg Asp Asn Lys Lys Thr Arg Ile Ile Pro Arg His Leu Gln Leu
            100                 105                 110

Ala Ile Arg Asn Asp Glu Glu Leu Asn Lys Leu Leu Gly Gly Val Thr
        115                 120                 125
```

Ile Ala Gln Gly Arg Arg Xaa Ala Gln His Pro Gly Arg Xaa Cys Cys
130 135 140

Pro Arg Arg Pro Ala Pro Pro Trp Gly Arg Xaa Pro Phe Gly Gly Gln
145 150 155 160

Glu Arg Ala Thr Lys Ala Ser Gln Gly Val Leu
165 170

<210> 463
<211> 433
<212> PRT
<213> Homo sapiens

<400> 463
Arg Val Arg Ala Pro Pro Arg Pro Pro Leu Gly Pro Ser Arg Pro Ser
1 5 10 15

His His Val His Pro Leu Gln Leu Pro Gly Ile Arg Glu Val Thr Ile
20 25 30

Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala Asp Pro Ser Leu
35 40 45

Gln Arg Val Arg Gln Glu Glu Ser Glu Gln Ile Lys Thr Leu Asn Asn
50 55 60

Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu Glu Gln Gln Asn
65 70 75 80

Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu Gln Lys Ser Ala
85 90 95

Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln Ile Ala Gly Leu
100 105 110

Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly Arg Leu Glu Ala
115 120 125

Glu Leu Arg Ser Met Gln Asp Val Val Glu Asp Phe Lys Asn Lys Tyr
130 135 140

Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn Glu Phe Val Val
145 150 155 160

Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys Val Glu Leu Glu
165 170 175

Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe Leu Arg Thr Leu
180 185 190

Asn Glu Thr Glu Leu Thr Glu Leu Gln Ser Gln Ile Ser Asp Thr Ser
195 200 205

Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp Leu Asp Gly Ile
210 215 220

Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala Lys Cys Ser Arg
225 230 235 240

Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu Thr Leu Gln Ala
245 250 255

Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr Arg Asn Glu Ile
260 265 270

Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala Glu Ile Asp Asn
275 280 285

Ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala Ile Ala Glu Ala Glu
290 295 300

Glu Arg Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala Lys Gln Glu Glu
305 310 315 320

Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met Ala Arg Gln Leu
325 330 335

Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala Leu Asp Ile Glu
340 345 350

Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser Arg Leu Ala
355 360 365

Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met Asn Ser Thr Gly
370 375 380

Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu Gly Gly Thr Met
385 390 395 400

Gly Ser Asn Ala Leu Ser Phe Ser Ser Ser Ala Gly Pro Gly Leu Leu
405 410 415

Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg Arg Ser Ala Arg
420 425 430

Asp

<210> 464
<211> 121
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (50)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (64)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (110)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (114)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (117)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 464
```
Gly Ser Gly Cys Val Phe Ala Ile Leu Gly Arg Arg Cys Ser Arg Pro
  1               5                  10                  15

Trp Arg Ile Trp Pro Gly Glu Pro Leu Gln Arg Ala Pro Pro Ala Ala
             20                  25                  30

Gly Thr Arg Trp Pro His Gly His Arg Ser Ser Pro Val Gly Thr Pro
         35                  40                  45

Gly Xaa Ala Pro Asn Val Pro Ala Ile Trp Gln Gln Pro Leu Trp Xaa
     50                  55                  60

Glu Tyr Ser Cys Glu Tyr Gly Ser Met Lys Phe Tyr Ala Leu Cys Gly
```

65 70 75 80

Phe Gly Gly Val Leu Ser Cys Gly Leu Thr His Thr Ala Val Val Pro
85 90 95

Leu Asp Leu Val Lys Cys Arg Met Gln Val Asp Pro Gln Xaa Tyr Lys
100 105 110

Gly Xaa Xaa Asn Xaa Ile Leu Ile Asn
115 120

<210> 465
<211> 68
<212> PRT
<213> Homo sapiens

<400> 465
Arg Ile Pro Ala Pro Ala Ser Ser Arg His Ser Gly Gly Arg Cys Ala
1 5 10 15

Ala Gly Pro Arg Gly Pro Pro Ala Thr Ala Ser Arg Ala Leu Arg Ala
20 25 30

Val His Arg Pro Leu Asp Ala Ala Arg Gly Arg Thr Gly Ser Thr Ser
35 40 45

His Leu Cys Ser Ser Ser Tyr Thr Ile Gly Cys Leu Leu Trp Phe Ser
50 55 60

Gln Lys Ala Met
65

<210> 466
<211> 224
<212> PRT
<213> Homo sapiens

<400> 466
Ala Thr Ile Leu Glu Arg Glu Ala Glu Gln Ser Arg Leu Gly Ala Thr
1 5 10 15

Glu Arg Ala Ala Ala Ala Ala Met Asn Pro Glu Tyr Asp Tyr Leu Phe
20 25 30

Lys Leu Leu Leu Ile Gly Asp Ser Gly Val Gly Lys Ser Cys Leu Leu
35 40 45

Leu Arg Phe Ala Asp Asp Thr Tyr Thr Glu Ser Tyr Ile Ser Thr Ile
50 55 60

Gly Val Asp Phe Lys Ile Arg Thr Ile Glu Leu Asp Gly Lys Thr Ile
65 70 75 80

Lys Leu Gln Ile Trp Asp Thr Ala Gly Gln Glu Arg Phe Arg Thr Ile
85 90 95

Thr Ser Ser Tyr Tyr Arg Gly Ala His Gly Ile Ile Val Val Tyr Asp
100 105 110

Val Thr Asp Gln Glu Ser Tyr Ala Asn Val Lys Gln Trp Leu Gln Glu
115 120 125

Ile Asp Arg Tyr Ala Ser Glu Asn Val Asn Lys Leu Leu Val Gly Asn
130 135 140

Lys Ser Asp Leu Thr Thr Lys Lys Val Val Asp Asn Thr Thr Ala Lys
145 150 155 160

Glu Phe Ala Asp Ser Leu Gly Ile Pro Phe Leu Glu Thr Ser Ala Lys
165 170 175

Asn Ala Thr Asn Val Glu Gln Ala Phe Met Thr Met Ala Ala Glu Ile
180 185 190

Lys Lys Arg Met Gly Pro Gly Ala Ala Ser Gly Gly Glu Arg Pro Asn
195 200 205

Leu Lys Ile Asp Ser Thr Pro Val Lys Pro Ala Gly Gly Gly Cys Cys
210 215 220

<210> 467
<211> 76
<212> PRT
<213> Homo sapiens

<400> 467
Ser Glu Ala Pro Gly Glu Ser Val Gly Thr Thr Pro Glu Ala Gln Met
1 5 10 15

Lys Thr Gly Pro Phe Ala Glu His Ser Asn Gln Leu Trp Asn Ile Ser
20 25 30

Ala Val Pro Ser Trp Ser Lys Val Asn Gln Gly Leu Ile Arg Met Tyr

35 40 45

Lys Ala Glu Cys Leu Glu Lys Phe Pro Val Ile Gln His Phe Lys Phe
50 55 60

Gly Ser Leu Leu Pro Ile His Pro Val Thr Ser Gly
65 70 75

<210> 468
<211> 111
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (47)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (97)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 468
Ser Leu Ala Arg Thr Gly Pro Arg Ser Leu Ala Arg Pro Cys Arg Arg
1 5 10 15

Arg Pro Ala His Arg His Pro Leu Gln Pro Cys Pro Pro Gly Xaa Cys
20 25 30

Pro Arg Xaa Pro Thr Ala Asp Val Arg Arg Pro Arg His Arg Xaa Arg
35 40 45

Xaa Glu Leu His Ala His Asn Val Thr Ser Pro Pro Ala Pro Thr Ala
50 55 60

Trp Ala Ala Pro Ala Pro Gln His Gln Pro Gln Pro Leu Xaa Leu Val
65 70 75 80

Pro Gly Arg Arg Val Cys Ser Arg Leu Leu Pro Arg Cys Ala Cys Gly
85 90 95

Xaa Cys Cys Pro Gly Val Ala Leu Ala Gly Arg Ile Pro Trp Asn
100 105 110

<210> 469
<211> 459
<212> PRT
<213> Homo sapiens

<400> 469
Pro Arg Val Arg Pro Arg Val Arg Pro Arg Val Arg Leu Ser Ser Pro
1 5 10 15

Ser Pro Val Cys Leu Pro Pro Ala Ala Ala Thr Met Thr Thr Ser Ile
20 25 30

Arg Gln Phe Thr Ser Ser Ser Ser Ile Lys Gly Ser Ser Gly Leu Gly
35 40 45

Gly Gly Ser Ser Arg Thr Ser Cys Arg Leu Ser Gly Gly Leu Gly Ala
50 55 60

Gly Ser Cys Arg Leu Gly Ser Ala Gly Gly Leu Gly Ser Thr Leu Gly
65 70 75 80

Gly Ser Ser Tyr Ser Ser Cys Tyr Ser Phe Gly Ser Gly Gly Gly Tyr
85 90 95

Gly Ser Ser Phe Gly Gly Val Asp Gly Leu Leu Ala Gly Gly Glu Lys
100 105 110

Ala Thr Met Gln Asn Leu Asn Asp Arg Leu Ala Ser Tyr Leu Asp Lys
115 120 125

Val Arg Ala Leu Glu Glu Ala Asn Thr Glu Leu Glu Val Lys Ile Arg
130 135 140

Asp Trp Tyr Gln Arg Gln Ala Pro Gly Pro Ala Arg Asp Tyr Ser Gln
145 150 155 160

Tyr Tyr Arg Thr Ile Glu Glu Leu Gln Asn Lys Ile Leu Thr Ala Thr
165 170 175

Val Asp Asn Ala Asn Ile Leu Leu Gln Ile Asp Asn Ala Arg Leu Ala
180 185 190

Ala Asp Asp Phe Arg Thr Lys Phe Glu Thr Glu Gln Ala Leu Arg Leu
195 200 205

Ser Val Glu Ala Asp Ile Asn Gly Leu Arg Arg Val Leu Asp Glu Leu
210 215 220

Thr Leu Ala Arg Ala Asp Leu Glu Met Gln Ile Glu Asn Leu Lys Glu
225 230 235 240

Glu Leu Ala Tyr Leu Lys Lys Asn His Glu Glu Glu Met Asn Ala Leu
245 250 255

Arg Gly Gln Val Gly Gly Glu Ile Asn Val Glu Met Asp Ala Ala Pro
260 265 270

Gly Val Asp Leu Ser Arg Ile Leu Asn Glu Met Arg Asp Gln Tyr Glu
275 280 285

Lys Met Ala Glu Lys Asn Arg Lys Asp Ala Glu Asp Trp Phe Phe Ser
290 295 300

Lys Thr Glu Glu Leu Asn Arg Glu Val Ala Thr Asn Ser Glu Leu Val
305 310 315 320

Gln Ser Gly Lys Ser Glu Ile Ser Glu Leu Arg Arg Thr Met Gln Ala
325 330 335

Leu Glu Ile Glu Leu Gln Ser Gln Leu Ser Met Lys Ala Ser Leu Glu
340 345 350

Gly Asn Leu Ala Glu Thr Glu Asn Arg Tyr Cys Val Gln Leu Ser Gln
355 360 365

Ile Gln Gly Leu Ile Gly Ser Val Glu Glu Gln Leu Ala Gln Leu Arg
370 375 380

Cys Glu Met Glu Gln Gln Asn Gln Glu Tyr Lys Ile Leu Leu Asp Val
385 390 395 400

Lys Thr Arg Leu Glu Gln Glu Ile Ala Thr Tyr Arg Arg Leu Leu Glu
405 410 415

```
Gly Glu Asp Ala His Leu Thr Gln Tyr Lys Lys Glu Pro Val Thr Thr
            420                 425                 430

Arg Gln Val Arg Thr Ile Val Glu Glu Val Gln Asp Gly Lys Val Ile
        435                 440                 445

Ser Ser Arg Glu Gln Val His Gln Thr Thr Arg
    450                 455



&lt;210&gt; 470
&lt;211&gt; 158
&lt;212&gt; PRT
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; SITE
&lt;222&gt; (158)
&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;400&gt; 470
Pro Pro Pro Pro Pro Pro Pro Glu Leu Cys Ser Met Ala Ser Arg Arg
  1               5                  10                  15

Met Glu Thr Lys Pro Val Ile Thr Cys Leu Lys Thr Leu Leu Ile Ile
             20                  25                  30

Tyr Ser Phe Val Phe Trp Ile Thr Gly Val Ile Leu Leu Ala Val Gly
         35                  40                  45

Val Trp Gly Lys Leu Thr Leu Gly Thr Tyr Ile Ser Leu Ile Ala Glu
     50                  55                  60

Asn Ser Thr Asn Ala Pro Tyr Val Leu Ile Gly Thr Gly Thr Thr Ile
 65                  70                  75                  80

Val Val Phe Gly Leu Phe Gly Cys Phe Ala Thr Cys Arg Gly Ser Pro
                 85                  90                  95

Trp Met Leu Lys Leu Tyr Ala Met Phe Leu Ser Leu Val Phe Leu Ala
            100                 105                 110

Glu Leu Val Ala Gly Ile Ser Gly Phe Val Phe Arg His Glu Ile Lys
        115                 120                 125

Asp Thr Phe Leu Arg Thr Tyr Thr Asp Ala Met Gln Thr Tyr Asn Gly
    130                 135                 140

Asn Asp Glu Arg Ser Arg Ala Val Asp His Val Gln Arg Xaa
145                 150                 155
```

<210> 471
<211> 59
<212> PRT
<213> Homo sapiens

<400> 471
Val Leu Phe Phe Tyr Glu Cys Pro Asn Leu Cys Phe Pro Leu Pro Ser
1 5 10 15

Gln Thr Val Trp Pro Val Glu Ser Val Trp Phe Val Phe Ile Ser Pro
20 25 30

Ser Phe Leu Glu Gln Gly Leu Arg Pro Cys His Ile Ser Tyr Ala Leu
35 40 45

His Pro Arg Leu Phe Trp Thr Leu Lys Val Asp
50 55

<210> 472
<211> 320
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (53)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 472
Asp Pro Asp Glu Val Phe Pro Val Cys Leu Pro Leu Thr Gly Asp Ala
1 5 10 15

```
Gly Glu Asp Gly Gly Lys Met Leu His Leu Pro Glu Trp Pro Glu Gln
            20                  25                  30

Pro Pro Gly Gly Pro Ala Ala Leu Gln Val Arg Gly Ala Glu Asp Xaa
        35                  40                  45

Xaa Leu Ser Phe Xaa Asp Cys Glu Ser Leu Gln Ala Val Phe Asp Pro
    50                  55                  60

Ala Ser Cys Pro His Met Leu Arg Ala Pro Ala Arg Val Leu Gly Glu
65                  70                  75                  80

Ala Val Leu Pro Phe Ser Pro Ala Leu Ala Glu Val Thr Leu Gly Ile
                85                  90                  95

Gly Arg Gly Ala Gly Ser Ser Trp Xaa Tyr His Glu Glu Glu Ala Asp
            100                 105                 110

Ser Thr Ala Lys Ala Met Val Thr Glu Met Cys Leu Gly Glu Glu Asp
        115                 120                 125

Phe Gln Gln Leu Gln Ala Gln Glu Gly Val Ala Ile Thr Phe Cys Leu
    130                 135                 140

Lys Glu Phe Arg Gly Leu Leu Ser Phe Ala Glu Ser Ala Asn Leu Asn
145                 150                 155                 160

Leu Ser Ile His Phe Asp Ala Pro Gly Arg Pro Ala Ile Phe Thr Ile
                165                 170                 175

Lys Asp Ser Leu Leu Asp Gly His Phe Val Leu Ala Thr Leu Ser Asp
            180                 185                 190

Thr Asp Ser His Ser Gln Asp Leu Gly Ser Pro Glu Arg His Gln Pro
        195                 200                 205

Val Pro Gln Leu Gln Ala His Ser Thr Pro His Pro Asp Asp Phe Ala
    210                 215                 220

Asn Asp Asp Ile Asp Ser Tyr Met Ile Ala Met Glu Thr Thr Ile Gly
225                 230                 235                 240

Asn Glu Gly Ser Arg Val Leu Pro Ser Ile Ser Leu Ser Pro Gly Pro
                245                 250                 255

Gln Pro Pro Lys Ser Pro Gly Pro His Ser Glu Glu Glu Asp Glu Ala
            260                 265                 270

Glu Pro Ser Thr Val Pro Gly Thr Pro Pro Pro Lys Lys Phe Arg Ser
        275                 280                 285
```

Leu Phe Phe Gly Ser Ile Leu Ala Pro Val Arg Ser Pro Gln Gly Pro
    290   295   300

Ser Leu Cys Trp Arg Lys Thr Val Arg Val Lys Ala Glu Pro Arg Thr
305   310   315   320

<210> 473
<211> 331
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (24)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (283)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (299)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (324)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 473
Pro Pro Cys Ala Val Pro Gly Pro Arg Leu Ser Pro Lys Leu Arg Thr
  1   5   10   15

Pro Ser Asn Ser Arg Glu Ser Xaa Ile Cys Val Ser Gly Arg Ala Glu
             20   25   30

Ala Leu Thr Phe Arg His Gly Ala Glu Gly Ser Asp Arg Arg Arg Gln
         35   40   45

Arg Arg Glu Gly Val Leu Gly Pro Ala Leu Leu Cys Arg Pro Trp Glu
     50   55   60

Val Leu Gly Ala His Glu Val Pro Ser Arg Asn Ile Phe Ser Glu Gln

65 70 75 80

Thr Ile Pro Pro Ser Ala Lys Tyr Gly Gly Arg His Thr Val Thr Met
85 90 95

Ile Pro Gly Asp Gly Ile Gly Pro Glu Leu Met Leu His Val Lys Ser
100 105 110

Val Phe Arg His Ala Cys Val Pro Val Asp Phe Glu Glu Val His Val
115 120 125

Ser Ser Asn Ala Asp Glu Glu Asp Ile Arg Asn Ala Ile Met Ala Ile
130 135 140

Arg Arg Asn Arg Val Ala Leu Lys Gly Asn Ile Glu Thr Asn His Asn
145 150 155 160

Leu Pro Pro Ser His Lys Ser Arg Asn Asn Ile Leu Arg Thr Ser Leu
165 170 175

Asp Leu Tyr Ala Asn Val Ile His Cys Lys Ser Leu Pro Gly Val Val
180 185 190

Thr Arg His Lys Asp Ile Asp Ile Leu Ile Val Arg Glu Asn Thr Glu
195 200 205

Gly Glu Tyr Ser Ser Leu Glu His Glu Ser Val Ala Gly Val Val Glu
210 215 220

Ser Leu Lys Ile Ile Thr Lys Ala Lys Ser Leu Arg Ile Ala Glu Tyr
225 230 235 240

Ala Phe Lys Leu Ala Gln Glu Ser Gly Arg Lys Lys Val Thr Ala Val
245 250 255

His Lys Ala Asn Ile Met Lys Leu Gly Asp Gly Leu Phe Leu Gln Cys
260 265 270

Cys Arg Glu Val Ala Ala Arg Tyr Pro Gln Xaa Thr Phe Glu Asn Met
275 280 285

Ile Val Asp Asn Thr Thr Met Gln Leu Val Xaa Arg Pro Gln Gln Phe
290 295 300

Asp Val Met Val Met Pro Asn Leu Tyr Gly Asn Ile Val Lys Gln Cys
305 310 315 320

Leu Arg Gly Xaa Gly Arg Gly Pro Lys Leu Val
325 330

<210> 474
<211> 30
<212> PRT
<213> Homo sapiens

<400> 474
Thr Pro Ile Ser Thr Lys Asn Thr Lys Ile Ser Gln Ala Arg Trp Arg
1 5 10 15

Ala His Val Val Pro Ala Thr Arg Glu Ala Asp Ala Glu Glu
20 25 30

<210> 475
<211> 124
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (110)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 475
Thr Gln Phe Ser Leu Ser Pro Val Glu Thr Ile Tyr Thr Ile Leu Cys
1 5 10 15

Ile Asn Val Tyr Thr Leu Pro Ile Cys Ile His Ile Tyr Ile Val Tyr
20 25 30

Ile Leu Tyr Met Tyr Arg Cys Val Tyr Val His Ile Tyr Thr His Ala
35 40 45

His Asn Lys Ile Arg Cys Ser Leu Gln Ile Gln Met Leu Ile Thr Lys
50 55 60

Pro Asp Ala Thr Gln Thr Ala Ala Glu Glu Thr Arg Leu Asp Ser Cys
65 70 75 80

Asn Arg Ser Gln Lys Ile Lys Thr Ala Thr Cys Ser Asp Phe Gly His
85 90 95

Phe Cys Met Phe Ile Lys Asn Gly Phe Val Thr Arg Lys Xaa Arg Thr
100 105 110

Ser Val Ser Glu Lys Gly Arg Trp Gly Glu Pro Ser
115 120

<210> 476
<211> 64
<212> PRT
<213> Homo sapiens

<400> 476
Asn Gly Tyr Leu Val Phe Pro Arg Lys Asn Ser Phe Leu Leu Ile Phe
1 5 10 15

Gly Leu Phe Val Tyr Leu Glu Thr Asn Leu Asp Ser Leu Pro Leu Val
20 25 30

Asp Thr His Ser Lys Arg Thr Leu Leu Ile Lys Thr Val Glu Thr Arg
35 40 45

Asp Gly Gln Val Ile Asn Glu Thr Ser Gln His His Asp Asp Leu Glu
50 55 60

<210> 477
<211> 107
<212> PRT
<213> Homo sapiens

<400> 477
Val Leu Thr Val Asp Ala Arg Asn His Gly Asp Ser Pro His Ser Pro
1 5 10 15

Asp Met Ser Tyr Glu Ile Met Ser Gln Asp Leu Gln Asp Leu Leu Pro
20 25 30

Gln Leu Gly Leu Val Pro Cys Val Val Val Gly His Ser Met Gly Gly
35 40 45

Lys Thr Ala Met Leu Leu Ala Leu Gln Arg Pro Glu Leu Val Glu Arg
50 55 60

Leu Ile Ala Val Asp Ile Ser Pro Val Glu Ser Thr Gly Val Ser His
65 70 75 80

Phe Ala Thr Tyr Val Ala Ala Met Arg Ala Ile Asn Ile Ala Asp Arg
85 90 95

Leu Ala Pro Leu Pro Cys Pro Lys Thr Gly Gly
100 105

<210> 478
<211> 282
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (281)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 478
```
Arg Glu Leu Gly Gly Thr Leu Leu Ser Ala Ile Glu Val Glu Gly Ala
  1               5                  10                  15

Lys Met Gln Ser Asn Lys Thr Phe Asn Leu Glu Lys Gln Asn His Thr
             20                  25                  30

Pro Arg Lys His His Gln His His His Gln Gln Gln His His Gln Gln
         35                  40                  45

Gln Gln Gln Gln Pro Pro Pro Pro Pro Ile Pro Ala Asn Gly Gln Gln
     50                  55                  60

Ala Ser Ser Gln Asn Glu Gly Leu Thr Ile Asp Leu Lys Asn Phe Arg
 65                  70                  75                  80

Lys Pro Gly Glu Lys Thr Phe Thr Gln Arg Ser Arg Leu Phe Val Gly
                 85                  90                  95

Asn Leu Pro Pro Asp Ile Thr Glu Glu Glu Met Arg Lys Leu Phe Glu
            100                 105                 110

Lys Tyr Gly Lys Ala Gly Glu Val Phe Ile His Lys Asp Lys Gly Phe
        115                 120                 125

Gly Phe Ile Arg Leu Glu Thr Arg Thr Leu Ala Glu Ile Ala Lys Val
    130                 135                 140

Glu Leu Asp Asn Met Pro Leu Arg Gly Lys Gln Leu Arg Val Arg Phe
145                 150                 155                 160

Ala Cys His Ser Ala Ser Leu Thr Val Arg Asn Leu Pro Gln Tyr Val
                165                 170                 175

Ser Asn Glu Leu Leu Glu Glu Ala Phe Ser Val Phe Gly Gln Val Glu
            180                 185                 190

Arg Ala Val Val Ile Val Asp Asp Arg Gly Arg Pro Ser Gly Lys Gly
        195                 200                 205
```

```
Ile Val Glu Phe Ser Gly Lys Pro Ala Ala Arg Lys Ala Leu Asp Arg
    210                 215                 220

Cys Ser Glu Gly Ser Phe Leu Leu Thr Thr Phe Pro Arg Pro Val Thr
225                 230                 235                 240

Val Glu Pro Met Asp Gln Leu Asp Asp Glu Glu Gly Leu Pro Glu Lys
                245                 250                 255

Leu Val Ile Lys Asn Gln Gln Phe His Lys Glu Arg Glu Gln Pro Pro
            260                 265                 270

Arg Phe Ala Gln Pro Gly Ser Phe Xaa Val
        275                 280
```

<210> 479
<211> 289
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (206)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (215)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (218)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (285)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 479

```
Ala Val Pro Val Arg Asn Ser Arg Val Asp Pro Arg Val Arg Val Cys
  1               5                  10                  15

Gly Pro Leu Ser Ala Pro Arg Gly Ser Arg Arg Pro Thr Val Pro Gly
             20                  25                  30

Thr Pro Ala Cys Leu Ala Arg Pro Ala Ala Gln Gly Phe Ser Ala Ala
```

35 40 45

Leu Pro Val Arg Trp Thr Gly Arg Arg Ala Gly Pro Ser Arg Pro Val
50 55 60

Pro Ile Gly Thr Pro Ser Arg Ala Ala Asp Pro Ser Gln Gly Glu Met
65 70 75 80

Ser Ala Asp Ala Ala Ala Gly Ala Pro Leu Pro Arg Leu Cys Cys Leu
85 90 95

Glu Lys Gly Pro Asn Gly Tyr Gly Phe His Leu His Gly Glu Lys Gly
100 105 110

Lys Leu Gly Gln Tyr Ile Arg Leu Val Glu Pro Gly Ser Pro Ala Glu
115 120 125

Lys Ala Gly Leu Leu Ala Gly Asp Arg Leu Val Glu Val Asn Gly Glu
130 135 140

Asn Val Glu Lys Glu Thr His Gln Gln Val Val Ser Arg Ile Arg Ala
145 150 155 160

Ala Leu Asn Ala Val Arg Leu Leu Val Val Asp Pro Glu Thr Asp Glu
165 170 175

Gln Leu Gln Lys Leu Gly Val Gln Val Arg Glu Glu Leu Leu Arg Ala
180 185 190

Gln Glu Ala Pro Gly Gln Ala Glu Pro Pro Ala Ala Ala Xaa Val Gln
195 200 205

Gly Ala Gly Asn Glu Asn Xaa Pro Arg Xaa Ala Asp Lys Ser His Pro
210 215 220

Glu Gln Arg Glu Leu Arg Pro Arg Leu Cys Thr Met Lys Lys Gly Pro
225 230 235 240

Ser Gly Tyr Gly Phe Asn Leu His Ser Asp Lys Ser Lys Pro Gly Gln
245 250 255

Phe Ile Arg Ser Val Asp Pro Asp Ser Pro Ala Glu Ala Ser Gly Leu
260 265 270

Arg Ala Gln Asp Arg Ile Val Glu Val Met Leu Leu Xaa Ser Leu Pro
275 280 285

Ile

<210> 480
<211> 44
<212> PRT
<213> Homo sapiens

<400> 480
Gly Ser Thr His Ala Ser Gly Arg Asn Glu Gly Pro Pro Ala Lys Thr
1 5 10 15

Lys Ser Trp Val Gly Pro Thr Leu His Phe His Arg Lys Ser Glu His
20 25 30

Leu Val Gly Leu Lys Val Leu Cys Cys Phe Arg Leu
35 40

<210> 481
<211> 124
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 481
Ser Ile Xaa His Xaa Arg Lys Xaa Xaa Xaa Thr Val Arg Ser Asp Ser
1 5 10 15

Arg Val Asp Pro Arg Ser Asp Asp Phe Thr Pro Leu Glu Ile Leu Trp
20 25 30

Thr Phe Ser Ile Tyr Leu Glu Ser Val Ala Ile Leu Pro Gln Leu Phe
35 40 45

Met Val Ser Lys Thr Gly Glu Ala Glu Thr Ile Thr Ser His Tyr Leu
50 55 60

Phe Ala Leu Gly Val Tyr Arg Thr Leu Tyr Leu Phe Asn Trp Ile Trp
65 70 75 80

Arg Tyr His Phe Glu Gly Phe Phe Asp Leu Ile Ala Ile Val Ala Gly
85 90 95

Leu Val Gln Thr Val Leu Tyr Cys Asp Phe Phe Tyr Leu Tyr Ile Thr
100 105 110

Lys Val Leu Lys Gly Lys Lys Leu Ser Leu Pro Ala
115 120

<210> 482
<211> 131
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (122)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (127)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (131)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 482
Cys Ser Ser Arg Gly Ala His His Ser His Cys Asp Arg Leu Pro His

```
 1               5                   10                  15

Ser Pro Trp Pro Gly Leu Arg Glu Val Glu Leu Leu Ala Ser Val His
            20                  25                  30

Thr Glu Gln Met Glu Glu Glu Leu Ala Leu Gly Pro Arg Gly Gln Gly
        35                  40                  45

Gly Ala Ser Leu Ala Gly Arg Asp Gly Arg Ser Ala Gly Ala Gly Ser
    50                  55                  60

Tyr Gly Ala Leu Ala Asn Ser Ala Trp Gly Gly Pro Arg Lys Val Ala
65                  70                  75                  80

Ser Ala Ser Ala Ala Ala Ser Thr Leu Ser Glu Pro Pro Arg Arg Thr
                85                  90                  95

Gln Glu Ser Arg Thr Arg Thr Arg Ala Leu Gly Leu Pro Thr Leu Pro
            100                 105                 110

Met Glu Lys Leu Ala Ala Ser Asn Arg Xaa Pro Xaa Gly Leu Xaa Gly
        115                 120                 125

Pro Gly Xaa
    130



<210> 483
<211> 221
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (168)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (174)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 483
Lys Lys Pro Pro Ile Thr His Pro Ser Thr Pro Ala Glu Glu Thr Tyr
 1               5                  10                  15

Asn Leu Gly Arg Gln Val Leu Pro Leu Ser Ala Val Thr Tyr Phe Gln
            20                  25                  30

Lys Ser Gly Pro Gly Leu Leu Pro Ala Pro Ala Thr Gln Ser Ala Ser
```

```
        35                  40                  45

Val Ala Gly Thr Leu Gln Asn Ser Leu Cys Ser Gln Val Thr Lys Lys
    50                  55                  60

Lys Arg Ala Asn Met Leu Val Leu Leu Ala Gly Ile Phe Val Val His
65                  70                  75                  80

Ile Ala Thr Val Ile Met Leu Phe Val Ser Thr Ile Ala Asn Val Trp
                85                  90                  95

Leu Val Ser Asn Thr Val Asp Ala Ser Val Gly Leu Trp Lys Asn Cys
            100                 105                 110

Thr Asn Ile Ser Cys Ser Asp Ser Leu Ser Tyr Ala Ser Glu Asp Ala
        115                 120                 125

Leu Lys Thr Val Gln Ala Phe Met Ile Leu Ser Ile Ile Phe Cys Val
    130                 135                 140

Ile Ala Leu Leu Val Phe Val Phe Gln Leu Phe Thr Met Glu Lys Gly
145                 150                 155                 160

Asn Arg Phe Phe Leu Ser Gly Xaa Thr Thr Leu Val Cys Xaa Leu Cys
                165                 170                 175

Ile Leu Val Gly Cys Pro Ser Thr Leu Val Ile Met Arg Ile Val Met
            180                 185                 190

Glu Arg Ile Cys Thr Thr Ala Ile Pro Thr Ser Trp Ala Gly Ser Ala
        195                 200                 205

Ser Ala Ser Ala Ser Ser Ser Ala Phe Ser Ile Trp Ser
    210                 215                 220


<210> 484
<211> 382
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (22)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (69)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (287)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (298)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (324)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (358)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 484
Thr Lys Leu Trp Thr Leu Val Ser Asn Pro Asp Thr Asp Ala Leu Ile
1   5   10   15

Cys Trp Ser Pro Ser Xaa Asn Ser Phe His Val Phe Asp Gln Gly Gln
            20   25   30

Phe Ala Lys Glu Val Leu Pro Lys Tyr Phe Lys His Asn Asn Met Ala
        35   40   45

Ser Phe Val Arg Gln Xaa Asn Met Tyr Gly Phe Arg Lys Val Val His
    50   55   60

Ile Glu Gln Gly Xaa Leu Val Lys Pro Glu Arg Asp Asp Thr Glu Phe
65   70   75   80

Gln His Pro Cys Phe Leu Arg Gly Gln Glu Gln Leu Leu Glu Asn Ile
                85   90   95

Lys Arg Lys Val Thr Ser Val Ser Thr Leu Lys Ser Glu Asp Ile Lys
            100   105   110

Ile Arg Gln Asp Ser Val Thr Lys Leu Leu Thr Asp Val Gln Leu Met
        115   120   125

```
Lys Gly Lys Gln Glu Cys Met Asp Ser Lys Leu Leu Ala Met Lys His
    130                 135                 140

Glu Asn Glu Ala Leu Trp Arg Glu Val Ala Ser Leu Arg Gln Lys His
145                 150                 155                 160

Ala Gln Gln Gln Lys Val Val Asn Lys Leu Ile Gln Phe Leu Ile Ser
                165                 170                 175

Leu Val Gln Ser Asn Arg Ile Leu Gly Val Lys Arg Lys Ile Pro Leu
            180                 185                 190

Met Leu Asn Asp Ser Gly Ser Ala His Ser Met Pro Lys Tyr Ser Arg
        195                 200                 205

Gln Phe Ser Leu Glu His Val His Gly Ser Gly Pro Tyr Ser Ala Pro
    210                 215                 220

Ser Pro Ala Tyr Ser Ser Ser Ser Leu Tyr Ala Pro Asp Ala Val Ala
225                 230                 235                 240

Ser Ser Gly Pro Ile Ile Ser Asp Ile Thr Glu Leu Ala Pro Ala Ser
                245                 250                 255

Pro Met Ala Ser Pro Gly Gly Ser Ile Asp Glu Arg Pro Leu Ser Ser
            260                 265                 270

Ser Pro Leu Val Arg Val Lys Glu Glu Pro Pro Ser Pro Pro Xaa Ser
        275                 280                 285

Pro Arg Val Glu Glu Ala Ser Pro Gly Xaa Pro Ser Ser Val Asp Thr
    290                 295                 300

Leu Leu Ser Pro Thr Ala Leu Ile Asp Ser Ile Leu Arg Glu Ser Glu
305                 310                 315                 320

Pro Ala Pro Xaa Ser Val Thr Ala Leu Thr Asp Ala Arg Gly His Thr
                325                 330                 335

Asp Thr Glu Gly Arg Pro Pro Ser Pro Pro Pro Thr Ser Thr Pro Glu
            340                 345                 350

Lys Cys Leu Ser Val Xaa Ala Trp Thr Arg Met Ser Ser Val Thr Thr
        355                 360                 365

Trp Met Leu Trp Thr Pro Thr Trp Ile Thr Cys Arg Pro Cys
    370                 375                 380
```

<210> 485

<211> 416
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (399)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 485

```
Pro Ser Val Ala Asn Val Gly Ser His Cys Asp Leu Ser Leu Lys Ile
  1               5                  10                  15

Pro Glu Ile Ser Ile Gln Asp Met Thr Ala Gln Val Thr Ser Pro Ser
             20                  25                  30

Gly Lys Thr His Glu Ala Glu Ile Val Glu Gly Glu Asn His Thr Tyr
         35                  40                  45

Cys Ile Arg Phe Val Pro Ala Glu Met Gly Thr His Thr Val Ser Val
     50                  55                  60

Lys Tyr Lys Gly Gln His Val Pro Gly Ser Pro Phe Gln Phe Thr Val
 65                  70                  75                  80

Gly Pro Leu Gly Glu Gly Gly Ala His Lys Val Arg Ala Gly Gly Pro
                 85                  90                  95

Gly Leu Glu Arg Ala Glu Ala Gly Val Pro Ala Glu Phe Ser Ile Trp
            100                 105                 110

Thr Arg Glu Ala Gly Ala Gly Gly Leu Ala Ile Ala Val Glu Gly Pro
        115                 120                 125

Ser Lys Ala Glu Ile Ser Phe Glu Asp Arg Lys Asp Gly Ser Cys Gly
    130                 135                 140

Val Ala Tyr Val Val Gln Glu Pro Gly Asp Tyr Glu Val Ser Val Lys
145                 150                 155                 160

Phe Asn Glu Glu His Ile Pro Asp Ser Pro Phe Val Val Pro Val Ala
                165                 170                 175

Ser Pro Ser Gly Asp Ala Arg Arg Leu Thr Val Ser Ser Leu Gln Glu
            180                 185                 190

Ser Gly Leu Lys Val Asn Gln Pro Ala Ser Phe Ala Val Ser Leu Asn
        195                 200                 205

Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His Ser Pro Ser Gly Ala
    210                 215                 220
```

Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln Asp Lys Tyr Ala Val
225 230 235 240

Arg Phe Ile Pro Arg Glu Asn Gly Val Tyr Leu Ile Asp Val Lys Phe
245 250 255

Asn Gly Thr His Ile Pro Gly Ser Pro Phe Lys Ile Arg Val Gly Glu
260 265 270

Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser Ala Tyr Gly Ala Gly
275 280 285

Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu Phe Val Val Asn Thr
290 295 300

Ser Asn Ala Gly Ala Gly Ala Leu Ser Val Thr Ile Asp Gly Pro Ser
305 310 315 320

Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu Gly Tyr Arg Val Thr
325 330 335

Tyr Thr Pro Met Ala Pro Gly Ser Tyr Leu Ile Ser Ile Lys Tyr Gly
340 345 350

Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys Ala Lys Val Thr Gly
355 360 365

Pro Arg Leu Val Ser Asn His Ser Leu His Glu Thr Ser Ser Val Phe
370 375 380

Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro Gln His Gly Xaa Pro
385 390 395 400

Gly Pro Gly Pro Ala Asp Ala Ser Lys Val Val Ala Lys Gly Trp Gly
405 410 415

<210> 486
<211> 46
<212> PRT
<213> Homo sapiens

<400> 486
Phe Val Thr Ser Gly Lys Ile Ser Leu Tyr Val Tyr Ile Leu Thr Ile
1 5 10 15

Arg Leu Asp Thr Asn Lys Ala Thr Leu Leu Thr Ala Ser Gly Glu Leu
20 25 30

Ile Leu Phe Leu Ile Phe Phe Asn Lys Asp Ile Leu Arg Tyr
35 40 45

<210> 487
<211> 162
<212> PRT
<213> Homo sapiens

<400> 487
Leu Gly Val Ala Leu Gly Ala Val Pro Lys Leu His Leu Gly Val Leu
1 5 10 15

Val Ser Thr Gly Leu Arg Thr Ala Val Gly Ser Pro Arg Leu Pro Pro
20 25 30

Thr Ala Leu Gly Ala Ala Tyr Gly Thr Ala Lys Ser Gly Thr Gly Ile
35 40 45

Ala Ala Met Ser Val Met Arg Pro Glu Gln Ile Met Lys Ser Ile Ile
50 55 60

Pro Val Val Met Ala Gly Ile Ile Ala Ile Tyr Gly Leu Val Val Ala
65 70 75 80

Val Leu Ile Ala Asn Ser Leu Asn Asp Asp Ile Ser Leu Tyr Lys Ser
85 90 95

Phe Leu Gln Leu Gly Ala Gly Leu Ser Val Gly Leu Ser Gly Leu Ala
100 105 110

Ala Gly Phe Ala Ile Gly Ile Val Gly Asp Ala Gly Val Arg Gly Thr
115 120 125

Ala Gln Gln Pro Arg Leu Phe Val Gly Met Ile Leu Ile Leu Ile Phe
130 135 140

Ala Glu Val Leu Gly Leu Tyr Gly Leu Ile Val Ala Leu Ile Leu Ser
145 150 155 160

Thr Lys

<210> 488
<211> 114

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (95)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (111)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (113)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 488
Gln Ala Leu Arg Pro Gly Ser Phe Arg Gly Thr Gly Arg Lys Arg Glu
1 5 10 15

Arg Glu Arg Glu Arg Met Ser Leu Ser Asp Trp His Leu Ala Val Lys
20 25 30

Leu Ala Asp Gln Pro Leu Ala Pro Lys Ser Ile Leu Gln Leu Pro Glu
35 40 45

Ser Glu Leu Gly Glu Tyr Ser Leu Gly Gly Tyr Ser Ile Ser Phe Leu
50 55 60

Lys Gln Leu Ile Ala Gly Lys Leu Gln Glu Ser Val Pro Asp Pro Glu
65 70 75 80

Leu Ile Asp Leu Ile Tyr Cys Gly Arg Lys Leu Lys Asp Asp Xaa Thr
85 90 95

Leu Thr Ser Thr Val Phe Asn Leu Ala Pro His Pro Cys Ser Xaa Glu
100 105 110

Xaa Leu

<210> 489
<211> 149
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (121)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (142)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 489

```
Ser Thr His Ala Ser Glu Asp Val Leu Ala Ala Pro Ser Gly Cys Arg
 1               5                  10                  15

Ala Ser Arg Pro Pro Thr Ser Gly Arg Glu Gln Phe Trp Ala Arg Gly
            20                  25                  30

Leu Ala Ala Ala Asp Met Thr Lys Gly Leu Val Leu Gly Ile Tyr Ser
        35                  40                  45

Lys Asp Lys Glu Asp Asp Val Pro Gln Phe Thr Ser Ala Gly Glu Asn
    50                  55                  60

Phe Asp Lys Leu Val Ser Gly Lys Leu Arg Glu Ile Leu Asn Ile Ser
65                  70                  75                  80

Gly Pro Pro Leu Lys Ala Gly Lys Thr Arg Thr Phe Tyr Gly Leu His
                85                  90                  95

Glu Asp Phe Pro Ser Val Val Val Val Gly Leu Gly Arg Lys Ala Ala
            100                 105                 110

Gly Val Asp Asp Gln Glu Asn Trp Xaa Glu Gly Lys Glu Asn Ile Arg
        115                 120                 125

Val Ala Met Gln Arg Gly Ala Gly Arg Phe Gln Asp Leu Xaa Ile Ser
    130                 135                 140

Ser Val Glu Gly Gly
145
```

<210> 490
<211> 527
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (311)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 490

Arg Arg Arg Ser Arg Gly Leu Ile Pro Gly Arg Ala Pro Gly Arg Arg
1 5 10 15

Arg Pro Arg Ala His Glu Val Ala Arg Ala Pro Pro Pro Ile Ala Met
20 25 30

Asp Arg Met Lys Lys Ile Lys Arg Gln Leu Ser Met Thr Leu Arg Gly
35 40 45

Gly Arg Gly Ile Asp Lys Thr Asn Gly Ala Pro Glu Gln Ile Gly Leu
50 55 60

Asp Glu Ser Gly Gly Gly Gly Gly Ser Asp Pro Gly Glu Ala Pro Thr
65 70 75 80

Arg Ala Ala Pro Gly Glu Leu Arg Ser Ala Arg Gly Pro Leu Ser Ser
85 90 95

Ala Pro Glu Ile Val His Glu Asp Leu Lys Met Gly Ser Asp Gly Glu
100 105 110

Ser Asp Gln Ala Ser Ala Thr Ser Ser Asp Glu Val Gln Ser Pro Val
115 120 125

Arg Val Arg Met Arg Asn His Pro Pro Arg Lys Ile Ser Thr Glu Asp
130 135 140

Ile Asn Lys Arg Leu Ser Leu Pro Ala Asp Ile Arg Leu Pro Glu Gly
145 150 155 160

Tyr Leu Glu Lys Leu Thr Leu Asn Ser Pro Ile Phe Asp Lys Pro Leu
165 170 175

Ser Arg Arg Leu Arg Arg Val Ser Leu Ser Glu Ile Gly Phe Gly Lys
180 185 190

Leu Glu Thr Tyr Ile Lys Leu Asp Lys Leu Gly Glu Gly Thr Tyr Ala
195 200 205

Thr Val Tyr Lys Gly Lys Ser Lys Leu Thr Asp Asn Leu Val Ala Leu
210 215 220

Lys Glu Ile Arg Leu Glu His Glu Glu Gly Ala Pro Cys Thr Ala Ile
225 230 235 240

Arg Glu Val Ser Leu Leu Lys Asp Leu Lys His Ala Asn Ile Val Thr
245 250 255

Leu His Asp Ile Ile His Thr Glu Lys Ser Leu Thr Leu Val Phe Glu

260 265 270

Tyr Leu Asp Lys Asp Leu Lys Gln Tyr Leu Asp Asp Cys Gly Asn Ile
275 280 285

Ile Asn Met His Asn Val Lys Leu Phe Leu Phe Gln Leu Leu Arg Gly
290 295 300

Leu Ala Tyr Cys His Arg Xaa Lys Val Leu His Arg Asp Leu Lys Pro
305 310 315 320

Gln Asn Leu Leu Ile Asn Glu Arg Gly Glu Leu Lys Leu Ala Asp Phe
325 330 335

Gly Leu Ala Arg Ala Lys Ser Ile Pro Thr Lys Thr Tyr Ser Asn Glu
340 345 350

Val Val Thr Leu Trp Tyr Arg Pro Pro Asp Ile Leu Leu Gly Ser Thr
355 360 365

Asp Tyr Ser Thr Gln Ile Asp Met Trp Gly Val Gly Cys Ile Phe Tyr
370 375 380

Glu Met Ala Thr Gly Arg Pro Leu Phe Pro Gly Ser Thr Val Glu Glu
385 390 395 400

Gln Leu His Phe Ile Phe Arg Ile Leu Gly Thr Pro Thr Glu Glu Thr
405 410 415

Trp Pro Gly Ile Leu Ser Asn Glu Glu Phe Lys Thr Tyr Asn Tyr Pro
420 425 430

Lys Tyr Arg Ala Glu Ala Leu Leu Ser His Ala Pro Arg Leu Asp Ser
435 440 445

Asp Gly Ala Asp Leu Leu Thr Lys Leu Leu Gln Phe Glu Gly Arg Asn
450 455 460

Arg Ile Ser Ala Glu Asp Ala Met Lys His Pro Phe Phe Leu Ser Leu
465 470 475 480

Gly Glu Arg Ile His Lys Leu Pro Asp Thr Thr Ser Ile Phe Ala Leu
485 490 495

Lys Glu Ile Gln Leu Gln Lys Glu Ala Ser Leu Arg Ser Ser Ser Met
500 505 510

Pro Asp Ser Gly Arg Pro Ala Phe Arg Val Val Asp Thr Glu Phe
515 520 525

<210> 491
<211> 125
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (125)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 491
```
Cys Thr Arg Ala His Pro Lys Asn Leu Val Glu Lys Gly Ile Leu Thr
  1               5                  10                  15

Thr Glu Lys Gln Asn Phe Leu Leu Phe Asp Met Thr Thr His Pro Val
             20                  25                  30

Thr Asn Thr Thr Glu Lys Gln Arg Leu Val Lys Lys Leu Gln Asp Ser
         35                  40                  45

Val Leu Glu Arg Trp Val Asn Asp Pro Gln Arg Met Asp Lys Arg Thr
     50                  55                  60

Leu Ala Leu Leu Val Leu Ala His Ser Ser Asp Val Leu Glu Asn Val
 65                  70                  75                  80

Phe Ser Ser Leu Thr Asp Asp Lys Tyr Asp Val Ala Met Asn Arg Ala
                 85                  90                  95

Lys Asp Leu Val Glu Leu Asp Pro Glu Val Glu Gly Thr Lys Pro Ser
            100                 105                 110

Ala Thr Glu Met Ile Trp Ala Val Leu Ala Ala Phe Xaa
        115                 120                 125
```

<210> 492
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (49)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (51)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 492
Val Ser Xaa Ser Ile Leu Ala Leu Leu Phe Asn Thr Asp Ala Leu Phe
1 5 10 15

Ser Arg Val Tyr Glu Ser Leu Ser Asp Asn His Gly Leu Gln Glu Gln
20 25 30

Thr Val Glu Lys Leu Phe Phe Gln Trp Lys Ser Trp Val Gln Glu Met
35 40 45

Xaa Gly Xaa Leu Lys
50

<210> 493
<211> 82
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (60)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (67)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (79)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 493
Pro Gly Phe Phe Phe Gln Met Leu Val His Thr Tyr Ser Ser Met Asp
1 5 10 15

Arg His Asp Gly Val Pro Ser His Ser Ser Arg Leu Ser Gln Leu Gly
20 25 30

Ser Val Ser Gln Gly Pro Tyr Ser Ser Ala Pro Pro Leu Ser His Thr
35 40 45

Pro Ser Ser Asp Phe Gln Pro Pro Tyr Phe Pro Xaa Pro Tyr Gln Pro
50 55 60

Leu Pro Xaa Xaa Gln Ser Gln Asp Pro Tyr Ser His Val Xaa Xaa Pro
65 70 75 80

Tyr Pro

<210> 494
<211> 290
<212> PRT
<213> Homo sapiens

<400> 494
Tyr Lys Asp Trp Leu Thr Lys Met Ser Gly Lys His Asp Val Gly Ala
1 5 10 15

Tyr Met Leu Met Tyr Lys Gly Ala Asn Arg Thr Glu Thr Val Thr Ser
20 25 30

Phe Arg Lys Arg Glu Ser Lys Val Pro Ala Asp Leu Leu Lys Arg Ala
35 40 45

Phe Val Arg Met Ser Thr Ser Pro Glu Ala Phe Leu Ala Leu Arg Ser
50 55 60

His Phe Ala Ser Ser His Ala Leu Ile Cys Ile Ser His Trp Ile Leu
65 70 75 80

Gly Ile Gly Asp Arg His Leu Asn Asn Phe Met Val Ala Met Glu Thr
85 90 95

Gly Gly Val Ile Gly Ile Asp Phe Gly His Ala Phe Gly Ser Ala Thr
100 105 110

Gln Phe Leu Pro Val Pro Glu Leu Met Pro Phe Arg Leu Thr Arg Gln
115 120 125

Phe Ile Asn Leu Met Leu Pro Met Lys Glu Thr Gly Leu Met Tyr Ser
130 135 140

Ile Met Val His Ala Leu Arg Ala Phe Arg Ser Asp Pro Gly Leu Leu
145 150 155 160

Thr Asn Thr Met Asp Val Phe Val Lys Glu Pro Ser Phe Asp Trp Lys
165 170 175

Asn Phe Glu Gln Lys Met Leu Lys Lys Gly Gly Ser Trp Ile Gln Glu
180 185 190

Ile Asn Val Ala Glu Lys Asn Trp Tyr Pro Arg Gln Lys Ile Cys Tyr
195 200 205

Ala Lys Arg Lys Leu Ala Gly Ala Asn Pro Ala Val Ile Thr Cys Asp
210 215 220

Glu Leu Leu Leu Gly His Glu Lys Ala Pro Ala Phe Arg Asp Tyr Val
225 230 235 240

Ala Val Ala Arg Gly Ser Lys Asp His Asn Ile Arg Ala Gln Glu Pro
245 250 255

Glu Ser Gly Leu Ser Glu Glu Thr Gln Val Lys Cys Leu Met Asp Gln
260 265 270

Ala Thr Asp Pro Asn Ile Leu Gly Arg Thr Trp Glu Gly Trp Glu Pro
275 280 285

Trp Met
290

<210> 495
<211> 156
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (148)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 495
Cys Gln Ser His Pro Leu Pro Gly Gly Pro Ala Cys Pro Cys Leu Ala
1 5 10 15

Cys His Ile Thr Leu Leu Phe Gly Arg Pro Trp Leu Ile Lys Glu Val

```
            20                  25                  30

Leu Val Val Ser Gln Ala Lys Trp Asn Leu Glu Thr Val Lys Lys Val
        35                  40                  45

Gln Ile Thr Leu Asn Cys Ile Gln Glu Val His Phe Phe Pro Ile Val
    50                  55                  60

Arg Gly Ser Trp Ser Leu Arg Asp Ala Arg Leu Glu Ser Asp Tyr Ile
65                  70                  75                  80

Ile Ile Gln Asn Gly Asn Ser Gln Gly Asn Ala Phe Phe His Phe Ile
                85                  90                  95

Arg Phe Phe Tyr Pro His Cys Thr Pro Ser Pro Ser Pro Leu Pro Ile
            100                 105                 110

Trp Met Ala Ser Gln Lys Leu Gly Pro Ser Pro Pro Cys Leu Gly Gly
        115                 120                 125

Gly Gln Ser Pro Leu Thr Ala Glu Ala Ala Leu Leu Ser Ser Ala Val
    130                 135                 140

Leu Pro Leu Xaa Lys Cys Leu Gln Arg Val Met Ser
145                 150                 155


<210> 496
<211> 251
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 496
Glu Glu Leu Leu Arg Ala Gln Glu Ala Pro Gly Gln Ala Glu Pro Pro
 1               5                  10                  15

Ala Ala Ala Glu Val Gln Gly Ala Gly Asn Glu Asn Glu Pro Arg Glu
            20                  25                  30

Ala Asp Lys Ser His Pro Glu Gln Arg Xaa Leu Arg Pro Arg Leu Cys
        35                  40                  45

Thr Met Lys Lys Gly Pro Ser Gly Tyr Gly Phe Asn Leu His Ser Asp
    50                  55                  60
```

Lys Ser Lys Pro Gly Gln Phe Ile Arg Ser Val Asp Pro Asp Ser Pro
65 70 75 80

Ala Glu Ala Ser Gly Leu Arg Ala Gln Asp Arg Ile Val Glu Val Asn
85 90 95

Gly Val Cys Met Glu Gly Lys Gln His Gly Asp Val Val Ser Ala Ile
100 105 110

Arg Ala Gly Gly Asp Glu Thr Lys Leu Leu Val Val Asp Arg Glu Thr
115 120 125

Asp Glu Phe Phe Lys Lys Cys Arg Val Ile Pro Ser Gln Glu His Leu
130 135 140

Asn Gly Pro Leu Pro Val Pro Phe Thr Asn Gly Glu Ile Gln Lys Glu
145 150 155 160

Asn Ser Arg Glu Ala Leu Ala Glu Ala Ala Leu Glu Ser Pro Arg Pro
165 170 175

Ala Leu Val Arg Ser Ala Ser Ser Asp Thr Ser Glu Glu Leu Asn Ser
180 185 190

Gln Asp Ser Pro Pro Lys Gln Asp Ser Thr Ala Pro Ser Ser Thr Ser
195 200 205

Ser Ser Asp Pro Ile Leu Asp Phe Asn Ile Ser Leu Ala Met Ala Lys
210 215 220

Glu Arg Ala His Gln Lys Arg Ser Ser Lys Arg Ala Pro Gln Met Asp
225 230 235 240

Trp Ser Lys Lys Asn Glu Leu Phe Ser Asn Leu
245 250

<210> 497
<211> 48
<212> PRT
<213> Homo sapiens

<400> 497
Asn Gly Ala Glu Ala Val Ser Thr Glu Ala Lys Met Thr Ala Phe Pro
1 5 10 15

Asp Trp Pro Trp Leu Phe His Thr Leu Cys Asp Pro Cys Pro Met Thr
20 25 30

Leu Trp Leu Thr Leu Pro Glu Ala Met Thr Thr Ala Ala Phe Cys His

35 40 45

<210> 498
<211> 373
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (337)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (372)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 498
Gly Thr Arg Gly Ser Arg Ala Ser Gly Val Cys Ala Arg Gly Cys Leu
1 5 10 15

Asp Ser Ala Gly Pro Trp Thr Met Ser Arg Ala Leu Arg Pro Pro Leu
20 25 30

Pro Pro Leu Cys Phe Phe Leu Leu Leu Leu Ala Ala Ala Gly Ala Arg
35 40 45

Ala Gly Gly Tyr Glu Thr Cys Pro Thr Val Gln Pro Asn Met Leu Asn
50 55 60

Val His Leu Leu Pro His Thr His Asp Asp Val Gly Trp Leu Lys Thr
65 70 75 80

Val Asp Gln Tyr Phe Tyr Gly Ile Lys Asn Asp Ile Gln His Ala Gly
85 90 95

Val Gln Tyr Ile Leu Asp Ser Val Ile Ser Ala Leu Leu Ala Asp Pro
100 105 110

Thr Arg Arg Phe Ile Tyr Val Glu Ile Ala Phe Phe Ser Arg Trp Trp
115 120 125

His Gln Gln Thr Asn Ala Thr Gln Glu Val Val Arg Asp Leu Val Arg
130 135 140

Gln Gly Arg Leu Glu Phe Ala Asn Gly Gly Trp Val Met Asn Asp Glu

145 150 155 160

Ala Ala Thr His Tyr Gly Ala Ile Val Asp Gln Met Thr Leu Gly Leu
165 170 175

Arg Phe Leu Glu Asp Thr Phe Gly Asn Asp Gly Arg Pro Arg Val Ala
180 185 190

Trp His Ile Asp Pro Phe Gly His Ser Arg Glu Gln Ala Ser Leu Phe
195 200 205

Ala Gln Met Gly Phe Asp Gly Phe Phe Phe Gly Arg Leu Asp Tyr Gln
210 215 220

Asp Lys Trp Val Arg Met Gln Lys Leu Glu Met Glu Gln Val Trp Arg
225 230 235 240

Ala Ser Thr Ser Leu Lys Pro Pro Thr Ala Asp Leu Phe Thr Gly Val
245 250 255

Leu Pro Asn Gly Tyr Asn Pro Pro Arg Asn Leu Cys Trp Asp Val Leu
260 265 270

Cys Val Asp Gln Pro Leu Val Glu Asp Pro Arg Ser Pro Glu Tyr Asn
275 280 285

Ala Lys Glu Leu Val Asp Tyr Phe Leu Asn Val Ala Thr Ala Gln Gly
290 295 300

Arg Tyr Tyr Arg Thr Asn His Thr Val Met Thr Met Gly Ser Asp Phe
305 310 315 320

Gln Tyr Glu Asn Ala Asn Met Trp Phe Lys Asn Leu Asp Lys Leu Ile
325 330 335

Xaa Leu Val Asn Ala Gln Gly Lys Arg Lys Gln Cys Pro Cys Ser Leu
340 345 350

Leu His Pro Arg Leu Leu Pro Leu Gly Ala Glu Gln Gly Gln Pro His
355 360 365

Leu Val Ser Xaa Thr
370

<210> 499
<211> 238
<212> PRT
<213> Homo sapiens

<400> 499

```
Ala Leu Pro Gly Pro Asp Trp His Gly Ala Gly Ala Ala Asp Arg Gly
1               5                   10                  15

Pro Ala Ala Pro Pro Arg Pro Gly Pro Cys Ala Tyr Ala Ala His Gly
            20                  25                  30

Arg Gly Ala Leu Ala Glu Ala Ala Arg Arg Cys Leu His Asp Ile Ala
        35                  40                  45

Leu Ala His Arg Ala Ala Thr Ala Ala Arg Pro Pro Ala Pro Pro Pro
    50                  55                  60

Ala Pro Gln Pro Pro Ser Pro Thr Pro Ser Pro Pro Arg Pro Thr Leu
65                  70                  75                  80

Ala Arg Glu Asp Asn Glu Glu Asp Glu Asp Glu Pro Thr Glu Thr Glu
                85                  90                  95

Thr Ser Gly Glu Gln Leu Gly Ile Ser Asp Asn Gly Gly Leu Phe Val
            100                 105                 110

Met Asp Glu Asp Ala Thr Leu Gln Asp Leu Pro Pro Phe Cys Glu Ser
        115                 120                 125

Asp Pro Glu Ser Thr Asp Asp Gly Ser Leu Ser Glu Glu Thr Pro Ala
    130                 135                 140

Gly Pro Pro Thr Cys Ser Val Pro Pro Ala Ser Ala Leu Pro Thr Gln
145                 150                 155                 160

Gln Tyr Ala Lys Ser Leu Pro Val Ser Val Pro Val Trp Gly Phe Lys
                165                 170                 175

Glu Lys Arg Thr Glu Ala Arg Ser Ser Asp Glu Glu Asn Gly Pro Pro
            180                 185                 190

Ser Ser Pro Asp Leu Asp Arg Ile Ala Ala Ser Met Arg Ala Leu Val
        195                 200                 205

Leu Arg Glu Ala Glu Asp Thr Gln Val Phe Gly Asp Leu Pro Arg Pro
    210                 215                 220

Arg Leu Asn Thr Ser Asp Phe Gln Lys Leu Lys Arg Lys Tyr
225                 230                 235
```

<210> 500
<211> 198
<212> PRT

<213> Homo sapiens

<220>
<221> SITE
<222> (94)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (156)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 500

```
Asn Ser Ala Glu Leu Ser Pro Gly Leu Cys Ser Pro Thr Pro Thr Glu
  1               5                  10                  15

Ala Arg Ala Gly Asp Ala Gly Pro Ala Ala Arg Ser Arg Lys Gln Asn
             20                  25                  30

Pro Gln Ser Pro Pro Cys Cys Cys Val Asp Asp Thr Trp Ala Gln Ala
         35                  40                  45

Glu Val Gly Pro Val Thr Ser Cys Thr Gly Phe Val Glu Gly Ser Ser
     50                  55                  60

Arg Thr Gly Gly Met Gly Ser Ala Cys Ile Lys Val Thr Lys Tyr Phe
 65                  70                  75                  80

Leu Phe Leu Phe Asn Leu Ile Phe Phe Ile Leu Gly Ala Xaa Ile Leu
                 85                  90                  95

Gly Phe Gly Val Trp Ile Leu Ala Asp Lys Ser Ser Phe Ile Ser Val
            100                 105                 110

Leu Gln Thr Ser Ser Ser Ser Leu Arg Met Gly Ala Tyr Val Phe Ile
        115                 120                 125

Gly Val Gly Ala Val Thr Met Leu Met Gly Phe Leu Gly Cys Ile Gly
    130                 135                 140

Ala Val Asn Glu Val Arg Cys Leu Leu Gly Leu Xaa Phe Ala Phe Leu
145                 150                 155                 160

Leu Leu Ile Leu Ile Ala Gln Val Thr Ala Gly Ala Leu Phe Tyr Phe
                165                 170                 175

Asn Met Gly Lys Val Ser Pro Ser Leu Pro Pro Ser Ser Leu Gly Trp
            180                 185                 190

Thr Asn His Gly Gly Asp
        195
```

<210> 501
<211> 169
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (165)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 501
Ser Ser Ala Ser Thr Asn Met Ser Arg Gly Ser Ser Ala Gly Phe Asp
1 5 10 15

Arg His Ile Thr Ile Phe Ser Pro Glu Gly Arg Leu Tyr Gln Val Glu
20 25 30

Tyr Ala Phe Lys Ala Ile Asn Gln Gly Gly Leu Thr Ser Val Ala Val
35 40 45

Arg Gly Lys Asp Cys Ala Val Ile Val Thr Gln Lys Lys Val Pro Asp
50 55 60

Lys Leu Leu Asp Ser Ser Thr Val Thr His Leu Phe Lys Ile Thr Glu
65 70 75 80

Asn Ile Gly Cys Val Met Thr Gly Met Thr Ala Asp Ser Arg Ser Gln
85 90 95

Val Gln Arg Ala Arg Tyr Glu Ala Ala Asn Trp Lys Tyr Lys Tyr Gly
100 105 110

Tyr Glu Ile Pro Val Asp Met Leu Cys Lys Arg Ile Ala Asp Ile Ser
115 120 125

Gln Val Tyr Thr Gln Asn Ala Glu Met Arg Pro Leu Gly Cys Cys Met
130 135 140

Ile Leu Ile Gly Ile Asp Glu Glu Gln Gly Pro Gln Val Tyr Lys Cys
145 150 155 160

Asp Pro Ala Gly Xaa Tyr Cys Gly Val
165

<210> 502
<211> 507

```
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (361)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (461)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 502
Val Arg Gln Leu Cys Arg Pro Ala Glu Xaa Asp Ser Val Met Ala Glu
  1               5                  10                  15

Gln Val Ala Leu Ser Arg Thr Gln Val Cys Gly Ile Leu Arg Glu Glu
             20                  25                  30

Leu Phe Gln Gly Asp Ala Phe His Gln Ser Asp Thr His Ile Phe Ile
         35                  40                  45

Ile Met Gly Ala Ser Gly Asp Leu Ala Lys Lys Lys Ile Tyr Pro Thr
     50                  55                  60

Ile Trp Trp Leu Phe Arg Asp Gly Leu Leu Pro Glu Asn Thr Phe Ile
 65                  70                  75                  80

Val Gly Tyr Ala Arg Ser Arg Leu Thr Val Ala Asp Ile Arg Lys Gln
                 85                  90                  95

Ser Glu Pro Phe Phe Lys Ala Thr Pro Glu Glu Lys Leu Lys Leu Glu
            100                 105                 110

Asp Phe Phe Ala Arg Asn Ser Tyr Val Ala Gly Gln Tyr Asp Asp Ala
        115                 120                 125

Ala Ser Tyr Gln Arg Leu Asn Ser His Met Asn Ala Leu His Leu Gly
    130                 135                 140

Ser Gln Ala Asn Arg Leu Phe Tyr Leu Ala Leu Pro Pro Thr Val Tyr
145                 150                 155                 160

Glu Ala Val Thr Lys Asn Ile His Glu Ser Cys Met Ser Gln Ile Gly
                165                 170                 175
```

Trp Asn Arg Ile Ile Val Glu Lys Pro Phe Gly Arg Asp Leu Gln Ser
180 185 190

Ser Asp Arg Leu Ser Asn His Ile Ser Ser Leu Phe Arg Glu Asp Gln
195 200 205

Ile Tyr Arg Ile Asp His Tyr Leu Gly Lys Glu Met Val Gln Asn Leu
210 215 220

Met Val Leu Arg Phe Ala Asn Arg Ile Phe Gly Pro Ile Trp Asn Arg
225 230 235 240

Asp Asn Ile Ala Cys Val Ile Leu Thr Phe Lys Glu Pro Phe Gly Thr
245 250 255

Glu Gly Arg Gly Gly Tyr Phe Asp Glu Phe Gly Ile Ile Arg Asp Val
260 265 270

Met Gln Asn His Leu Leu Gln Met Leu Cys Leu Val Ala Met Glu Lys
275 280 285

Pro Ala Ser Thr Asn Ser Asp Asp Val Arg Asp Glu Lys Val Lys Val
290 295 300

Leu Lys Cys Ile Ser Glu Val Gln Ala Asn Asn Val Val Leu Gly Gln
305 310 315 320

Tyr Val Gly Asn Pro Asp Gly Glu Gly Glu Ala Thr Lys Gly Tyr Leu
325 330 335

Asp Asp Pro Thr Val Pro Arg Gly Ser Thr Thr Ala Thr Phe Ala Ala
340 345 350

Val Val Leu Tyr Val Glu Asn Glu Xaa Trp Asp Gly Val Pro Phe Ile
355 360 365

Leu Arg Cys Gly Lys Ala Leu Asn Glu Arg Lys Ala Glu Val Arg Leu
370 375 380

Gln Phe His Asp Val Ala Gly Asp Ile Phe His Gln Gln Cys Lys Arg
385 390 395 400

Asn Glu Leu Val Ile Arg Val Gln Pro Asn Glu Ala Val Tyr Thr Lys
405 410 415

Met Met Thr Lys Lys Pro Gly Met Phe Phe Asn Pro Glu Glu Ser Glu
420 425 430

Leu Asp Leu Thr Tyr Gly Asn Arg Tyr Lys Asn Val Lys Leu Pro Asp
435 440 445

```
Ala Tyr Glu Arg Leu Ile Leu Asp Val Phe Cys Gly Xaa Gln Met His
    450                 455                 460

Phe Val Arg Arg Thr Ser Ser Val Arg Pro Gly Val Phe Ser Pro His
465                 470                 475                 480

Cys Cys Thr Arg Leu Ser Trp Arg Ser Pro Ser Pro Ser Pro Ile Phe
                485                 490                 495

Met Ala Ala Glu Ala Pro Arg Arg Gln Thr Ser
            500                 505
```

<210> 503
<211> 260
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 503

```
Gly Pro Glu Val Leu Pro Glu Pro Arg Val Pro Arg Glu Ala Leu Ala
  1               5                  10                  15

Phe Ile Ile Arg Ser Phe Gly Gly Glu Val Ser Trp Asp Lys Ser Leu
            20                  25                  30

Cys Ile Gly Ala Thr Tyr Asp Val Thr Asp Ser Arg Ile Thr His Gln
        35                  40                  45

Ile Val Asp Arg Pro Gly Gln Gln Thr Ser Val Ile Gly Arg Cys Tyr
    50                  55                  60

Val Gln Pro Gln Xaa Val Phe Asp Ser Val Asn Ala Arg Leu Leu Leu
65                  70                  75                  80

Pro Val Ala Glu Tyr Phe Ser Gly Val Gln Leu Pro Pro His Leu Ser
                85                  90                  95

Pro Phe Val Thr Glu Lys Glu Gly Asp Tyr Val Pro Pro Glu Lys Leu
            100                 105                 110

Lys Leu Leu Ala Leu Gln Arg Gly Glu Asp Pro Gly Asn Leu Asn Glu
        115                 120                 125

Ser Glu Glu Glu Glu Glu Glu Asp Asp Asn Asn Glu Gly Asp Gly Asp
```

130 135 140

Glu Glu Gly Glu Asn Glu Glu Glu Glu Glu Asp Ala Glu Ala Gly Ser
145 150 155 160

Glu Lys Glu Glu Glu Ala Arg Leu Ala Ala Leu Glu Glu Gln Arg Met
165 170 175

Glu Gly Lys Lys Pro Arg Val Met Ala Gly Thr Leu Lys Leu Glu Asp
180 185 190

Lys Gln Arg Leu Ala Gln Glu Glu Glu Ser Glu Ala Lys Arg Leu Ala
195 200 205

Ile Met Met Met Lys Lys Arg Glu Lys Tyr Leu Tyr Gln Lys Ile Met
210 215 220

Phe Gly Lys Arg Arg Lys Ile Arg Glu Ala Asn Lys Leu Ala Glu Lys
225 230 235 240

Arg Lys Ala His Asp Glu Ala Val Arg Ser Glu Lys Lys Ala Lys Lys
245 250 255

Ala Arg Pro Glu
260

<210> 504
<211> 424
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (292)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (342)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 504
Leu Leu Gln Arg Cys Tyr Ala Phe Pro Gly His Arg Leu Ala His Ser
1 5 10 15

Gly Ser Asp Leu Ser Leu Leu Val Pro Glu Ile Glu Asp Met Tyr Ser
20 25 30

Ser Pro Tyr Leu Arg Pro Ser Glu Ser Pro Ile Thr Val Glu Val Asn

35 40 45

Cys Thr Asn Pro Gly Thr Arg Tyr Cys Trp Met Ser Thr Gly Leu Tyr
50 55 60

Ile Pro Gly Arg Gln Ile Ile Glu Val Ser Leu Pro Glu Ala Ala Ala
65 70 75 80

Ser Ala Asp Leu Lys Ile Gln Ile Gly Cys His Thr Asp Asp Leu Thr
85 90 95

Arg Ala Ser Lys Leu Phe Arg Gly Pro Leu Val Ile Asn Arg Cys Cys
100 105 110

Leu Asp Lys Pro Thr Lys Ser Ile Thr Cys Leu Trp Gly Gly Leu Leu
115 120 125

Tyr Ile Ile Val Pro Gln Asn Ser Lys Leu Gly Ser Val Pro Val Thr
130 135 140

Val Lys Gly Ala Val His Ala Pro Tyr Tyr Lys Leu Gly Glu Thr Thr
145 150 155 160

Leu Glu Glu Trp Lys Arg Arg Ile Gln Glu Asn Pro Gly Pro Trp Gly
165 170 175

Glu Leu Ala Thr Asp Asn Ile Ile Leu Thr Val Pro Thr Ala Asn Leu
180 185 190

Arg Thr Leu Glu Asn Pro Glu Pro Leu Leu Arg Leu Trp Asp Glu Val
195 200 205

Met Gln Ala Val Ala Arg Leu Gly Ala Glu Pro Phe Pro Leu Arg Leu
210 215 220

Pro Gln Arg Ile Val Ala Asp Val Gln Ile Ser Val Gly Trp Met His
225 230 235 240

Ala Gly Tyr Pro Ile Met Cys His Leu Glu Ser Val Gln Glu Leu Ile
245 250 255

Asn Glu Lys Leu Ile Arg Thr Lys Gly Leu Trp Gly Pro Val His Glu
260 265 270

Leu Gly Arg Asn Gln Gln Arg Gln Glu Trp Glu Phe Pro Pro His Thr
275 280 285

Thr Glu Ala Xaa Cys Asn Leu Trp Cys Val Tyr Val His Glu Thr Val
290 295 300

Leu Gly Ile Pro Arg Ser Arg Ala Asn Ile Ala Leu Trp Pro Pro Val

305 310 315 320

Arg Glu Lys Arg Val Arg Ile Tyr Leu Ser Lys Gly Pro Asn Val Lys
325 330 335

Asn Trp Asn Ala Trp Xaa Ala Leu Glu Thr Tyr Leu Gln Leu Gln Glu
340 345 350

Ala Phe Gly Trp Glu Pro Phe Ile Arg Leu Phe Thr Glu Tyr Arg Asn
355 360 365

Gln Thr Asn Leu Pro Thr Glu Asn Val Asp Lys Met Asn Leu Trp Val
370 375 380

Lys Met Phe Ser His Gln Val Gln Lys Asn Leu Ala Pro Phe Phe Glu
385 390 395 400

Ala Trp Ala Gly Pro Ser Arg Arg Lys Trp Leu Pro Ala Trp Pro Ile
405 410 415

Cys Leu Asn Gly Arg Lys Ile Leu
420

<210> 505
<211> 70
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (66)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (70)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 505

Leu His Gln Ser Leu Leu His Leu Glu Lys Thr Asn Glu Arg Lys Ser
1 5 10 15

Ile Phe Leu Ile His Tyr Pro Asn Asn Asn Arg Thr Pro Tyr Arg Asn
20 25 30

Tyr Tyr His Tyr Val Ser Lys His Tyr Ile Pro Ile Thr Tyr Pro Thr
35 40 45

Xaa Ser Ile Ile Asp Xaa Ile Ser Ile Pro Thr Met Ile Ser Ala Leu
50 55 60

Asn Xaa Gln Asn Lys Xaa
65 70

<210> 506
<211> 434
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (363)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 506
Ser Thr His Ala Ser Ala His Ala Ser Val Ser Thr Ala Ala Ala Ala
1 5 10 15

Ala Leu Ala Ala Ala Ala Val Lys Ala Lys His Leu Ala Ala Val Glu
20 25 30

Glu Arg Lys Ile Lys Ser Leu Val Ala Leu Leu Val Glu Thr Gln Met
35 40 45

Lys Lys Leu Glu Ile Lys Leu Arg His Phe Glu Glu Leu Glu Thr Ile
50 55 60

Met Asp Arg Glu Xaa Glu Ala Leu Glu Tyr Gln Arg Gln Gln Leu Leu

65 70 75 80

Ala Asp Arg Gln Ala Phe His Met Glu Gln Leu Lys Tyr Ala Glu Met
85 90 95

Arg Ala Arg Gln Gln His Phe Gln Gln Met His Gln Gln Gln Gln Gln
100 105 110

Pro Pro Pro Ala Leu Pro Pro Gly Ser Gln Pro Ile Pro Pro Thr Gly
115 120 125

Ala Ala Gly Pro Pro Ala Xaa His Gly Leu Ala Val Ala Pro Ala Ser
130 135 140

Val Val Pro Ala Pro Ala Gly Ser Gly Ala Pro Pro Gly Ser Leu Gly
145 150 155 160

Pro Ser Glu Gln Ile Gly Gln Ala Gly Ser Thr Ala Gly Pro Gln Gln
165 170 175

Gln Gln Pro Ala Gly Ala Pro Gln Pro Gly Ala Val Pro Pro Gly Val
180 185 190

Pro Pro Pro Gly Pro His Gly Pro Ser Pro Phe Pro Asn Gln Gln Thr
195 200 205

Pro Pro Ser Met Met Pro Gly Ala Val Pro Gly Ser Gly His Pro Gly
210 215 220

Val Ala Gly Asn Ala Pro Leu Gly Leu Pro Phe Gly Met Pro Pro Pro
225 230 235 240

Pro Pro Pro Pro Ala Pro Ser Ile Ile Pro Phe Gly Ser Leu Ala Asp
245 250 255

Ser Ile Ser Ile Asn Leu Pro Ala Pro Pro Asn Leu His Gly His His
260 265 270

His His Leu Pro Phe Ala Pro Gly Thr Leu Pro Pro Pro Asn Leu Pro
275 280 285

Val Ser Met Ala Asn Pro Leu His Pro Asn Leu Pro Ala Thr Thr Thr
290 295 300

Met Pro Ser Ser Leu Pro Leu Gly Pro Gly Leu Gly Ser Ala Ala Ala
305 310 315 320

Gln Ser Pro Ala Ile Val Ala Ala Val Gln Gly Asn Leu Leu Pro Ser
325 330 335

Ala Ser Pro Leu Pro Asp Pro Gly Thr Pro Leu Pro Pro Asp Pro Thr

340 345 350

Ala Pro Ser Pro Arg His Gly His Pro Cys Xaa His Leu His Ser Glu
355 360 365

Glu Pro Ala Arg His Leu Ser Pro Ser Pro Pro Val Asp Ile Thr Val
370 375 380

Pro Gly Thr Ala Leu Pro Pro Pro Leu Gly Pro Ser Pro Ala Trp Arg
385 390 395 400

Val His His Tyr Val Arg Lys Ala Pro Ser Ala Pro Pro Lys Pro Ser
405 410 415

Pro Cys Leu Thr Glu Ala Cys Ile Phe Ile Ser Asp Tyr Ser Arg Thr
420 425 430

Ser Val

<210> 507
<211> 303
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (165)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (280)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 507
Glu Tyr Val Phe Pro Ala Lys Lys Lys Leu Gln Glu Tyr Arg Val Leu
1 5 10 15

Ile Thr Thr Leu Ile Thr Ala Gly Ser Trp Ser Arg Pro Ser Phe Pro
20 25 30

Leu Ile Thr Ser His Thr Ser Ser Ser Met Arg Leu Ala Thr Ala Trp
35 40 45

Ser Leu Arg Ser Leu Val Ala Ile Ala Gly Leu Met Glu Val Lys Glu
50 55 60

Thr Gly Asp Pro Gly Gly Gln Leu Val Leu Ala Gly Asp Pro Arg Gln

65 70 75 80

Leu Gly Pro Val Leu Arg Ser Pro Leu Thr Gln Lys His Gly Leu Gly
85 90 95

Tyr Ser Leu Leu Glu Arg Leu Leu Thr Tyr Asn Ser Leu Tyr Lys Lys
100 105 110

Gly Pro Asp Gly Tyr Asp Pro Gln Phe Ile Thr Lys Leu Leu Arg Asn
115 120 125

Tyr Arg Ser His Pro Thr Ile Leu Asp Ile Pro Asn Gln Leu Tyr Tyr
130 135 140

Glu Gly Glu Leu Gln Ala Cys Ala Asp Val Val Asp Arg Glu Arg Phe
145 150 155 160

Cys Arg Trp Ala Xaa Leu Pro Arg Gln Gly Phe Pro Ile Ile Phe His
165 170 175

Gly Val Met Gly Lys Asp Glu Arg Glu Gly Asn Ser Pro Ser Phe Phe
180 185 190

Asn Pro Glu Glu Ala Ala Thr Val Thr Ser Tyr Leu Lys Leu Leu Leu
195 200 205

Ala Pro Ser Ser Lys Lys Gly Lys Ala Arg Leu Ser Pro Arg Ser Val
210 215 220

Gly Val Ile Ser Pro Tyr Arg Lys Gln Val Glu Lys Ile Arg Tyr Cys
225 230 235 240

Ile Thr Lys Leu Asp Arg Glu Leu Arg Gly Leu Asp Asp Ile Lys Asp
245 250 255

Leu Lys Val Gly Ser Val Glu Glu Phe Gln Gly Gln Glu Arg Ser Val
260 265 270

Ile Leu Ile Ser Thr Val Arg Xaa Ala Arg Ala Leu Cys Ser Trp Ile
275 280 285

Trp Thr Leu Ile Trp Val Ser Leu Arg Thr Pro Arg Gly Ser Met
290 295 300

<210> 508
<211> 250
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 508
```
Glu Gln Tyr Leu Pro Leu Thr Glu Glu Glu Leu Glu Lys Glu Ala Xaa
  1               5                  10                  15

Lys Val Glu Gly Phe Asp Leu Val Gln Lys Pro Ser Tyr Tyr Val Arg
             20                  25                  30

Leu Gly Ser Leu Ser Thr Lys Leu His Ser Arg Ala Tyr Gln Gln Ala
         35                  40                  45

Leu Ser Arg Val Lys Glu Ala Lys Gln Lys Ser Gln Gln Thr Ile Ser
     50                  55                  60

Gln Leu His Ser Thr Val His Leu Ile Glu Phe Ala Arg Lys Asn Val
 65                  70                  75                  80

Tyr Ser Ala Asn Gln Lys Ile Gln Asp Ala Gln Asp Lys Leu Tyr Leu
                 85                  90                  95

Ser Trp Val Glu Trp Lys Arg Ser Ile Gly Tyr Asp Asp Thr Asp Glu
            100                 105                 110

Ser His Cys Ala Glu His Ile Glu Ser Arg Thr Leu Ala Ile Ala Arg
        115                 120                 125

Asn Leu Thr Gln Gln Leu Gln Thr Thr Cys His Thr Leu Leu Ser Asn
    130                 135                 140

Ile Gln Gly Val Pro Gln Asn Ile Gln Asp Gln Ala Lys His Met Gly
145                 150                 155                 160

Val Met Ala Gly Asp Ile Tyr Ser Val Phe Arg Asn Ala Ala Ser Phe
                165                 170                 175

Lys Glu Val Ser Asp Ser Leu Leu Thr Ser Ser Lys Gly Gln Leu Gln
            180                 185                 190

Lys Met Lys Glu Ser Leu Asp Asp Val Met Asp Tyr Leu Val Asn Asn
        195                 200                 205

Thr Pro Leu Asn Trp Leu Val Gly Pro Phe Tyr Pro Gln Leu Thr Glu
    210                 215                 220

Ser Gln Asn Ala Gln Asp Gln Gly Ala Glu Met Asp Lys Ser Ser Gln
225                 230                 235                 240
```

Glu Thr Gln Arg Ser Glu His Lys Thr His
245 250

<210> 509
<211> 98
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (97)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 509
His Glu Leu Trp Gly Cys Gly Pro Val Thr Pro Arg Arg Thr Ala Pro
1 5 10 15

Ser Gly Trp Ala Gln Ala Pro Leu Ser Asp Thr Ala Gln Val Tyr Met
20 25 30

Glu Leu Gln Gly Leu Val Asp Pro Gln Ile Gln Leu Pro Leu Leu Ala
35 40 45

Ala Arg Ser Thr Ser Cys Arg Ser Ser Leu Ile Ala Ser Gln Pro Gly
50 55 60

Pro His Gln Lys Gly Arg Gln Gly Leu Arg Gly Asn Lys Ser Phe Leu
65 70 75 80

Pro Ser Ser Trp Asn Cys Gln Asn Trp Thr Arg Gln Pro Leu Thr Ser
85 90 95

Xaa Ser

<210> 510
<211> 392
<212> PRT
<213> Homo sapiens

<400> 510
Gly Ala Met Arg Gly Asp Arg Gly Arg Gly Arg Gly Gly Arg Phe Gly
1 5 10 15

Ser Arg Gly Gly Pro Gly Gly Gly Phe Arg Pro Phe Val Pro His Ile
20 25 30

Pro Phe Asp Phe Tyr Leu Cys Glu Met Ala Phe Pro Arg Val Lys Pro
35 40 45

Ala Pro Asp Glu Thr Ser Phe Ser Glu Ala Leu Leu Lys Arg Asn Gln
50 55 60

Asp Leu Ala Pro Asn Ser Ala Glu Gln Ala Ser Ile Leu Ser Leu Val
65 70 75 80

Thr Lys Ile Asn Asn Val Ile Asp Asn Leu Ile Val Ala Pro Gly Thr
85 90 95

Phe Glu Val Gln Ile Glu Glu Val Arg Gln Val Gly Ser Tyr Lys Lys
100 105 110

Gly Thr Met Thr Thr Gly His Asn Val Ala Asp Leu Val Val Ile Leu
115 120 125

Lys Ile Leu Pro Thr Leu Glu Ala Val Ala Ala Leu Gly Asn Lys Val
130 135 140

Val Glu Ser Leu Arg Ala Gln Asp Pro Ser Glu Val Leu Thr Met Leu
145 150 155 160

Thr Asn Glu Thr Gly Phe Glu Ile Ser Ser Ser Asp Ala Thr Val Lys
165 170 175

Ile Leu Ile Thr Thr Val Pro Pro Asn Leu Arg Lys Leu Asp Pro Glu
180 185 190

Leu His Leu Asp Ile Lys Val Leu Gln Ser Ala Leu Ala Ala Ile Arg
195 200 205

His Ala Arg Trp Phe Glu Glu Asn Ala Ser Gln Ser Thr Val Lys Val
210 215 220

Leu Ile Arg Leu Leu Lys Asp Leu Arg Ile Arg Phe Pro Gly Phe Glu
225 230 235 240

Pro Leu Thr Pro Trp Ile Leu Asp Leu Leu Gly His Tyr Ala Val Met
245 250 255

Asn Asn Pro Thr Arg Gln Pro Leu Ala Leu Asn Val Ala Tyr Arg Arg
260 265 270

Cys Leu Gln Ile Leu Ala Ala Gly Leu Phe Leu Pro Gly Ser Val Gly
275 280 285

Ile Thr Asp Pro Cys Glu Ser Gly Asn Phe Arg Val His Thr Val Met
290 295 300

Thr Leu Glu Gln Gln Asp Met Val Cys Tyr Thr Ala Gln Thr Leu Val
305 310 315 320

Arg Ile Leu Ser His Gly Gly Phe Arg Lys Ile Leu Gly Gln Glu Gly
325 330 335

Asp Ala Ser Tyr Leu Ala Ser Glu Ile Ser Thr Trp Asp Gly Val Ile
340 345 350

Val Thr Pro Ser Glu Lys Ala Tyr Glu Lys Pro Pro Glu Lys Lys Glu
355 360 365

Gly Glu Glu Glu Glu Glu Asn Thr Glu Glu Pro Pro Gln Gly Glu Glu
370 375 380

Glu Glu Ser Met Glu Thr Gln Glu
385 390

<210> 511
<211> 72
<212> PRT
<213> Homo sapiens

<400> 511
His Gly Gly Gly Lys Gly Arg Gln Val Gly Leu His Ser Val Gln Arg
1 5 10 15

Pro Ala Arg Arg Glu Thr Ala Ala Ser Trp Gly Leu Cys Val Lys Ile
20 25 30

Pro Asp Leu Gly Val Ala Phe Val Tyr Lys Met Gln Glu Gly Lys Pro
35 40 45

Val Pro Asp Ser Ser Arg Gln His Ala Gln Leu Ser Gly Ser Pro Val
50 55 60

Ser Gln Gly Leu Ser Leu Pro Leu
65 70

<210> 512
<211> 181
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (14)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (33)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 512
```
Gly Trp Cys Ser Cys Ala His Ser Ser Ala Trp Pro Gly Xaa Trp Gly
  1               5                  10                  15

Ala Ser Gly Ile Pro Gln Gln Ala Pro Met Thr Val Cys Asp Gln Ala
             20                  25                  30

Xaa Pro Val Thr Phe Leu Leu Leu His Leu Glu Gly Gly Asp Ile His
         35                  40                  45

Thr Val Ser His Leu Ser Ser Pro Pro Pro Gly Val Ala His Arg Met
     50                  55                  60

Gly Thr Gly Gly Ser Arg Asn Pro Asn Pro Ala Trp Leu Gly Gly Ala
 65                  70                  75                  80

Leu Leu Val Arg Gly Arg Pro Ala Ser Leu Ala Pro Trp Gly His Ser
                 85                  90                  95

Trp Lys Arg Gly Leu Ala His Ala Pro Leu Arg Ala Gly Thr Cys Thr
            100                 105                 110

Gly His Thr Arg His Ser Ala Cys Trp Asn Arg Trp Leu Cys Ser Cys
        115                 120                 125

Ser Gly Pro Arg Ala Ala Xaa Leu Arg Pro Cys Thr Ser His Met His
    130                 135                 140

Trp Thr Arg Ala Glu Thr Pro Val Cys Tyr Arg Ala Leu Val Leu Cys
145                 150                 155                 160

Gly Pro Gly Ala Thr Ala Gln Ser Ser Gln Trp Arg Ser Thr Pro Leu
                165                 170                 175

Asp Ser Ile Phe Phe
            180
```

<210> 513
<211> 202
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 513
```
Leu Gly Asp Thr Ile Glu Gly Thr Pro Ala Gly Thr Val Pro Xaa Phe
  1               5                  10                  15

Pro Gly Arg Pro Thr Arg Ala Ile Met Ala Gln Asp Gln Gly Glu Lys
             20                  25                  30

Glu Asn Pro Met Arg Glu Leu Arg Ile Arg Lys Leu Cys Leu Asn Ile
         35                  40                  45

Cys Val Gly Glu Ser Gly Asp Arg Leu Thr Arg Ala Ala Lys Val Leu
     50                  55                  60

Glu Gln Leu Thr Gly Gln Thr Pro Val Phe Ser Lys Ala Arg Tyr Thr
 65                  70                  75                  80

Val Arg Ser Phe Gly Ile Arg Arg Asn Glu Lys Ile Ala Val His Cys
                 85                  90                  95

Thr Val Arg Gly Ala Lys Ala Glu Glu Ile Leu Glu Lys Gly Leu Lys
            100                 105                 110

Val Arg Glu Tyr Glu Leu Arg Lys Asn Asn Phe Ser Asp Thr Gly Asn
        115                 120                 125

Phe Gly Phe Gly Ile Gln Glu His Ile Asp Leu Gly Ile Lys Tyr Asp
    130                 135                 140

Pro Ser Ile Gly Ile Tyr Gly Leu Asp Phe Tyr Val Val Leu Gly Arg
145                 150                 155                 160

Pro Gly Phe Ser Ile Ala Asp Lys Lys Arg Arg Thr Gly Cys Ile Gly
                165                 170                 175

Ala Lys His Arg Ile Ser Lys Glu Glu Ala Met Arg Trp Phe Gln Gln
            180                 185                 190

Lys Tyr Asp Gly Ile Ile Leu Pro Gly Lys
        195                 200
```

<210> 514
<211> 63
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 514
```
Xaa Xaa Lys Asn Xaa Ile Thr Pro Lys Glu Glu Ser Pro Pro His Xaa
 1               5                  10                  15

Ala Leu Leu Ser Lys Cys Leu Leu Thr Pro Ser Pro Lys Met Pro Pro
            20                  25                  30

Ile Leu Xaa Val Met Ala Ala Leu Gly Phe Glu Arg Arg Glu Phe Gly
        35                  40                  45

Ser Thr Ser Val Glu Arg Val Gln Ser Arg Gln Leu Asp Cys Phe
    50                  55                  60
```

<210> 515
<211> 218
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (151)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (209)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (211)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 515
```
Ser Leu Ala Arg Gly Cys Gln Arg Pro Asp Ala Val Leu Tyr Ala Arg
  1               5                  10                  15

His Tyr Asn Ile Pro Val Ile His Ala Phe Arg Arg Ala Val Asp Asp
             20                  25                  30

Pro Gly Leu Val Phe Asn Gln Leu Pro Lys Met Leu Tyr Pro Glu Tyr
         35                  40                  45

His Lys Val His Gln Met Met Arg Glu Gln Ser Ile Leu Ser Pro Ser
     50                  55                  60

Pro Tyr Glu Gly Tyr Arg Ser Leu Pro Arg His Gln Leu Leu Cys Phe
 65                  70                  75                  80

Lys Glu Asp Cys Gln Ala Val Phe Gln Asp Leu Glu Gly Val Glu Lys
                 85                  90                  95

Val Phe Gly Val Ser Leu Val Leu Val Leu Ile Gly Ser His Pro Asp
            100                 105                 110

Leu Ser Phe Leu Pro Gly Ala Gly Ala Asp Phe Ala Val Asp Pro Asp
        115                 120                 125

Gln Pro Leu Ser Ala Lys Arg Asn Pro Ile Asp Val Asp Pro Phe Thr
    130                 135                 140

Tyr Gln Ser Thr Arg Gln Xaa Gly Leu Tyr Ala Met Gly Pro Leu Ala
145                 150                 155                 160

Gly Asp Asn Phe Val Arg Phe Val Gln Gly Gly Ala Leu Ala Val Ala
                165                 170                 175

Ser Ser Leu Leu Arg Lys Glu Gln Asn His Leu His Arg Gln Pro Trp
            180                 185                 190
```

```
Ser Ser Leu Arg Gly Ile His Pro Leu Ile Asp Leu Lys Ser Gly Val
        195                 200                 205

Xaa Pro Xaa Leu Val Lys Leu Thr Ala Gln
    210                 215
```

```
<210> 516
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (22)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 516
Asn Gly Arg Pro Asp Ser Thr Gly Pro Ala Ile Pro Gly Ile Leu Ser
  1               5                  10                  15

Trp Gly Phe Glu Thr Xaa Leu Arg Asp Arg Glu Thr Asp Pro Arg Asn
             20                  25                  30

Val Leu Asn Cys Asn Gly Pro His Thr
         35                  40
```

```
<210> 517
<211> 250
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (118)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (161)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (204)
<223> Xaa equals any of the naturally occurring L-amino acids
```

<400> 517

```
Gly Phe Asn Arg Ser Phe Cys Gly Arg Asn Ala Thr Val Tyr Gly Lys
  1               5                  10                  15

Gly Val Tyr Phe Ala Arg Arg Ala Ser Leu Ser Val Gln Asp Arg Tyr
             20                  25                  30

Ser Pro Pro Asn Ala Asp Gly His Lys Ala Val Phe Val Ala Arg Val
         35                  40                  45

Leu Thr Gly Asp Tyr Gly Gln Gly Arg Arg Gly Leu Arg Ala Pro Pro
     50                  55                  60

Leu Arg Gly Pro Gly His Val Leu Leu Arg Tyr Asp Ser Ala Val Asp
 65                  70                  75                  80

Cys Ile Cys Gln Pro Ser Ile Phe Val Ile Phe His Asp Thr Gln Ala
                 85                  90                  95

Leu Pro Thr His Leu Ile Thr Cys Glu Ala Arg Ala Pro Arg Phe Pro
            100                 105                 110

Arg Arg Pro Leu Trp Xaa Pro Gly Pro Leu Pro Arg His Leu Thr Glu
        115                 120                 125

Gly Ala Thr Leu Trp Pro Pro Ala Ser Gln Ala Pro Ser Ser Ala Gln
    130                 135                 140

Ala Asp Ala Pro Arg Pro Gln Leu Trp Pro Pro Glu Leu Ser Pro Gly
145                 150                 155                 160

Xaa Pro Cys Leu Pro Leu Arg Ala Pro Glu Gly Gly Val Gly Asp Gly
                165                 170                 175

Gly Gln Gln Arg Pro Arg Gly Ala Gly Leu Gly Pro Ser Leu Gly Arg
            180                 185                 190

Pro His His Gln Gly Ser Ala Glu Pro Arg Arg Xaa His Arg Pro Pro
        195                 200                 205

Ala Ala Pro Arg Pro Arg Pro Ser Arg Leu Cys Cys Leu Asn Lys Arg
    210                 215                 220

Glu Arg Glu Pro Arg Arg Lys Gly Pro Gly Lys Lys Lys Lys Lys Lys
225                 230                 235                 240

Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
                245                 250
```

<210> 518
<211> 100
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 518
```
Asn Pro Xaa Lys Lys Leu Xaa Ile Leu Ile Lys Trp Pro Pro Pro Phe
  1               5                  10                  15

Pro Pro Ser Phe Pro Pro Ser Pro Asn Ser Leu Ser Ser Ser Ser Phe
             20                  25                  30

Pro Pro Pro Leu Ser Leu Phe Ser Pro Ser Phe Thr Phe Leu Ile Ser
         35                  40                  45

Val Lys Leu Glu Arg Phe Glu Ile Pro Ile Lys Val Arg Leu Ser Pro
     50                  55                  60

Glu Pro Trp Thr Pro Glu Thr Gly Leu Val Thr Asp Ala Phe Lys Leu
 65                  70                  75                  80

Lys Arg Lys Glu Leu Arg Asn His Tyr Leu Lys Asp Ile Glu Arg Met
                 85                  90                  95

Tyr Gly Gly Lys
            100
```

<210> 519
<211> 60
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (17)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 519
His Glu Asp Gly Xaa Leu Met Gly Cys Arg His Arg Trp His Pro Arg
1 5 10 15

Xaa Val Pro Phe His Gln Thr Ser Pro Lys Thr Glu Leu Glu Ser Thr
20 25 30

Ile Phe Gly Ser Pro Arg Leu Ala Ser Gly Leu Phe Pro Glu Trp Gln
35 40 45

Ser Trp Gly Arg Met Glu Asn Leu Ala Ser Tyr Arg
50 55 60

<210> 520
<211> 120
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 520
Ser His Pro Tyr Ala Pro Ser Cys Gly Leu Arg Gly Pro Gly Ala Ala
1 5 10 15

Ser Arg Ala Arg Thr Arg Glu Arg Xaa Pro Gln Ala Glu Ala Glu Ala
20 25 30

Arg Ser Thr Pro Gly Pro Ala Gly Ser Arg Leu Gly Pro Glu Thr Phe
35 40 45

Arg Gln Arg Phe Arg Gln Phe Arg Tyr Gln Asp Ala Ala Gly Pro Arg
50 55 60

Glu Ala Phe Arg Gln Leu Arg Glu Leu Ser Arg Gln Trp Leu Arg Pro
65 70 75 80

Asp Ile Arg Thr Lys Glu Gln Ile Val Glu Met Leu Val Gln Glu Gln
85 90 95

Leu Leu Ala Ile Leu Pro Glu Ala Ala Arg Ala Arg Arg Ile Arg Arg
100 105 110

Arg Thr Asp Val Arg Ile Thr Gly

115 120

<210> 521
<211> 96
<212> PRT
<213> Homo sapiens

<400> 521
Gly His Gln Thr Val Ser Pro Ser Thr Gly Ser Arg Val Thr Arg Met
1 5 10 15

Phe Ser Leu Ile Ser Phe Ser His Val Phe Ile Lys Asp Ile Cys Lys
20 25 30

Leu Pro Lys Asp Glu Gly Thr Cys Arg Asp Phe Ile Leu Lys Trp Tyr
35 40 45

Tyr Asp Pro Asn Thr Lys Ser Cys Ala Arg Phe Trp Tyr Gly Gly Cys
50 55 60

Gly Gly Asn Glu Asn Lys Phe Gly Ser Gln Lys Glu Cys Glu Lys Val
65 70 75 80

Cys Ala Pro Val Leu Ala Lys Pro Gly Val Ile Ser Val Met Gly Thr
85 90 95

<210> 522
<211> 122
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 522
Asn Ser Gly Phe Arg Pro Lys Asn Pro Val Gly Arg Gly Gly Glu Pro
1 5 10 15

Glu Xaa Cys Gly Gly Ala Gly Gly Leu Gly Cys Thr Leu Val Trp Gly
20 25 30

Gly Thr Gly Ala Ala Val Val Thr Gly Val Val Trp Leu Leu Leu Pro

35 40 45

Asn Gly Gly Val Gly Val Gly Leu Leu Gly Pro Gln Ser Pro Val Gly
50 55 60

Gly Ser Asp Ser Ala Pro Tyr Ser Leu His Pro Ala Gly Arg Thr Trp
65 70 75 80

Gly Leu Arg Ser Glu Cys Ile Pro Pro Leu Ser Phe Asn Leu Ser Cys
85 90 95

Arg Thr His Ser Gly Pro Gly Ala Arg Leu Gly Glu Ala Gly Pro Asn
100 105 110

Tyr Gly Ser Arg Glu Leu Gln Val Pro Thr
115 120

<210> 523
<211> 94
<212> PRT
<213> Homo sapiens

<400> 523
Leu Ile Pro Gln Val Cys Cys Lys His Ser Met Glu Asp Thr Asp Asp
1 5 10 15

Ser Leu Val Leu Val Phe Leu Ser Ala Val Asn Val Gln Gln Phe Ala
20 25 30

Gln Glu Leu Gly Asp His Ile Cys Leu Ser Gly Gln Gly Ser Glu Val
35 40 45

His Trp Asn Leu Leu Arg Asn Leu Phe Val Lys Thr Ile Val Asn Asn
50 55 60

Tyr Cys Ile Phe Leu Gln Lys Tyr Ile Leu Glu Asn Cys Ile Leu Ser
65 70 75 80

Ile Lys Val Phe Leu Cys Lys Lys Lys Lys Lys Lys Leu Val
85 90

<210> 524
<211> 93
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (86)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (93)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 524

```
Ser Ala Val Met Gly Arg Lys Lys Lys Lys Gln Leu Lys Pro Trp Cys
  1               5                  10                  15

Trp Tyr Cys Asn Arg Asp Phe Asp Asp Glu Lys Ile Leu Ile Gln His
             20                  25                  30

Gln Lys Ala Lys His Phe Lys Cys His Ile Cys His Lys Lys Leu Tyr
        35                  40                  45

Thr Gly Pro Gly Leu Ala Ile His Cys Met Gln Val His Lys Glu Thr
    50                  55                  60

Ile Asp Ala Val Pro Asn Ala Tyr Leu Gly Glu Gln Thr Xaa Ile Gly
 65                  70                  75                  80

Asn Ile Trp Tyr Gly Xaa Tyr Ser Arg Lys Arg Tyr Xaa
                 85                  90
```

<210> 525
<211> 324
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (323)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 525

```
Asp Leu Arg Leu Ser Arg Pro Glu Ala Val Glu Ala Glu Ala Met Met
  1               5                  10                  15

Ala Ala Met Ala Thr Ala Arg Val Arg Met Gly Pro Arg Cys Ala Gln
             20                  25                  30
```

Ala Leu Trp Arg Met Pro Trp Leu Pro Val Phe Leu Ser Leu Ala Ala
35 40 45

Ala Ala Ala Ala Ala Ala Ala Glu Gln Gln Val Pro Leu Val Leu Trp
50 55 60

Ser Ser Asp Arg Asp Leu Trp Ala Pro Ala Ala Asp Thr His Glu Gly
65 70 75 80

His Ile Thr Ser Asp Leu Gln Leu Ser Thr Tyr Leu Asp Pro Ala Leu
85 90 95

Glu Leu Gly Pro Arg Asn Val Leu Leu Phe Leu Gln Asp Lys Leu Ser
100 105 110

Ile Glu Asp Phe Thr Ala Tyr Gly Gly Val Phe Gly Asn Lys Gln Asp
115 120 125

Ser Ala Phe Ser Asn Leu Glu Asn Ala Leu Asp Leu Ala Pro Ser Ser
130 135 140

Leu Val Leu Pro Ala Val Asp Trp Tyr Ala Val Ser Thr Leu Thr Thr
145 150 155 160

Tyr Leu Gln Glu Lys Leu Gly Ala Ser Pro Leu His Val Asp Leu Ala
165 170 175

Thr Leu Arg Glu Leu Lys Leu Asn Ala Ser Leu Pro Ala Leu Leu Leu
180 185 190

Ile Arg Leu Pro Tyr Thr Ala Ser Ser Gly Leu Met Ala Pro Arg Glu
195 200 205

Val Leu Thr Gly Asn Asp Glu Val Ile Gly Gln Val Leu Ser Thr Leu
210 215 220

Lys Ser Glu Asp Val Pro Tyr Thr Ala Ala Leu Thr Ala Val Arg Pro
225 230 235 240

Ser Arg Val Ala Arg Asp Val Ala Val Val Ala Gly Gly Leu Gly Arg
245 250 255

Gln Leu Leu Gln Lys Gln Pro Val Ser Pro Val Ile His Pro Pro Val
260 265 270

Ser Tyr Asn Asp Thr Ala Pro Arg Ile Leu Phe Trp Ala Gln Asn Phe
275 280 285

Ser Val Ala Tyr Lys Asp Gln Trp Glu Asp Leu Thr Pro Leu Thr Phe
290 295 300

Gly Val Gln Glu Leu Asn Leu Thr Gly Ser Phe Trp Asn Asp Ser Phe
305 310 315 320

Ala Ser Xaa His

<210> 526
<211> 66
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 526
Phe Xaa Val Ser Trp Thr Trp Lys Gln Val Ser Glu Phe Pro Gly Asp
1 5 10 15

Gln Arg Asp Glu Val Leu Gln Leu Pro Pro Ser Ser Cys Asn Leu Val
20 25 30

Ser Ser Gly Ala Gly Gly Glu Pro Glu Lys Leu Ala Ser Tyr Ile Thr
35 40 45

Ser Leu Trp Leu Phe Phe Ile Cys Lys Thr Arg Ile Ile Leu Asn Cys
50 55 60

Lys Gly
65

<210> 527
<211> 62
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (40)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 527
Asn Thr Gln Leu Trp Phe Leu Cys Phe Pro Asn Cys Lys Ala Ala Asp
1 5 10 15

```
Asn Lys Thr Pro Gly Phe His Val Ser Ser Ala Met Ser Thr Leu Thr
            20                  25                  30

Gln Ile Leu Lys Gln Asn Ser Xaa Asn Ala Val Leu Arg Ile Gln Leu
        35                  40                  45

Leu Leu Lys Pro Ile Ser Ile Cys Ile Ile Thr Thr Asn Ile
    50                  55                  60



<210> 528
<211> 122
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (80)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (104)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 528
Tyr Asn Lys Ile Glu Ile Met His Leu Val Met Trp Pro Thr Ser Leu
  1               5                  10                  15

Leu Thr Thr Met Asp Cys Phe Gln Gln Gln Leu Ile Phe Trp Ser Val
            20                  25                  30

Leu Arg Gly Ala Cys Met Ser Phe Val Thr Ser Gly Ser Thr Pro Ala
        35                  40                  45

Val Lys Tyr Cys Phe His Leu Pro Leu Gln Lys Ala Ser Cys Leu Leu
    50                  55                  60

Thr Ser Thr Ala Lys Ala Leu Phe Trp Thr Gly Tyr Leu Ile Lys Xaa
 65                  70                  75                  80

Ile Ser Val Arg Leu Cys Ser Val Ile Pro Ser Glu Pro Arg Phe Val
                 85                  90                  95

Ser Lys Ala Thr Val Leu Ser Xaa Xaa Pro Cys Val Trp Gly Gln Val
```

100 105 110

Ala Ile Pro Pro Met Ser Leu Val Ile Leu
115 120

<210> 529
<211> 182
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 529
Asp Arg Thr Arg Leu Ser Gln Ala Ser Thr Pro Thr Pro Val Cys Trp
1 5 10 15

Gly Leu Leu Gln Pro Pro Pro Trp Xaa Glu Ala Trp Tyr Arg Leu Thr
20 25 30

His Arg Gly Leu Cys Gln Val Arg Phe Cys Arg Trp Ser Gln Ala Leu
35 40 45

Pro Glu Ala Arg Gly Gly Ala Trp Ala Gly Ser Pro Gly Glu Gly Gln
50 55 60

Ala Gly Pro Arg Leu His Thr His Ile Gln Pro Ala Gly Leu Ser Ala
65 70 75 80

Val Leu Ser Pro Ser Leu Ser Ser Pro Ser Ser Ala Val Thr Leu Ser
85 90 95

Ser Pro Ser Leu Pro Ala Ser Pro Pro Ala Ala Pro Pro Val Lys Arg
100 105 110

Met Thr Lys Asp Leu Ser Tyr Ala Gly Ser Lys Asn Gln Asn Phe Leu
115 120 125

Leu Ala Phe Ser Phe Val Ala Ser Pro Ala Pro Ala Leu Pro Val Ser
130 135 140

His Pro Gly Pro Arg Leu Glu Ala Ser Leu His Leu Ser Tyr Cys Phe
145 150 155 160

Lys Pro Lys Phe Thr Val Ser Val Gly Gly Gln Asp Leu Leu Ser Pro
165 170 175

Pro Leu Leu His Pro Pro
180

<210> 530
<211> 183
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (79)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (80)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (81)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 530
Ala Leu Val Leu Gly Xaa Lys Ser Val Arg Met Ala Ser Ser Arg Met
1 5 10 15

Thr Arg Arg Asp Pro Leu Thr Asn Lys Val Ala Leu Val Thr Ala Ser
20 25 30

Thr Asp Gly Ile Gly Phe Ala Ser Pro Gly Val Trp Pro Arg Thr Gly
35 40 45

Pro Arg Gly Arg Gln Gln Pro Glu Ala Ala Glu Cys Gly Pro Gly Gly
50 55 60

Gly Thr Leu Gln Gly Glu Gly Leu Ser Val Thr Gly Thr Cys Xaa Xaa
65 70 75 80

Xaa Gly Lys Ala Glu Asp Arg Glu Arg Leu Val Ala Thr Ala Val Lys
85 90 95

Leu His Gly Gly Ile Asp Ile Leu Val Ser Asn Ala Ala Val Asn Pro
100 105 110

Phe Phe Gly Ser Ile Met Asp Val Thr Glu Glu Val Trp Asp Lys Leu
115 120 125

Trp Met Asp Lys Glu Lys Glu Glu Ser Met Lys Glu Thr Leu Arg Ile
130 135 140

Arg Arg Leu Gly Glu Pro Glu Asp Cys Ala Gly Ile Val Ser Phe Leu
145 150 155 160

Cys Ser Glu Asp Ala Ser Tyr Ile Thr Gly Glu Thr Val Val Val Gly
165 170 175

Gly Gly Thr Pro Ser Arg Leu
180

<210> 531
<211> 129
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (89)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (103)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 531
Asn Ser Ala Pro Leu Ser Pro Thr Gly Leu Gly Gln Gly His Thr Gly
1 5 10 15

His Val Arg Phe Leu Ala Ala Val Gln Leu Pro Asp Gly Phe Asn Leu
20 25 30

Leu Cys Pro Thr Pro Pro Pro Pro Pro Asp Thr Gly Pro Glu Lys Leu
35 40 45

Pro Ser Leu Glu His Arg Asp Ser Pro Trp His Arg Gly Pro Ala Pro
50 55 60

Ala Arg Pro Lys Met Leu Val Ile Ser Gly Gly Asp Gly Tyr Glu Asp
65 70 75 80

Phe Arg Leu Ser Ser Gly Gly Gly Xaa Ala Val Arg Leu Trp Val Glu
85 90 95

Thr Thr Ala Gln Thr Thr Xaa Ser Cys Gly Gly Cys Asp Pro Val Cys
100 105 110

Arg Gly Pro Gly Leu Ala Arg Pro Pro Ala Phe Ser Leu Leu Ala Ser
115 120 125

Pro

<210> 532
<211> 91
<212> PRT
<213> Homo sapiens

<400> 532
Gly Ala Ile Ala Ser Ser Gly Pro Thr Gly Gly Arg Val Arg Lys His
1 5 10 15

Gln Leu Leu Pro Gly Ala Val Arg Glu Trp Glu Gln Leu Trp Ala Pro
20 25 30

His Phe Arg Gln Val Leu Pro Lys Pro Ser Asp Ala Val Arg Pro Gly
35 40 45

Leu Pro Val Val Leu Phe Arg Leu Cys Phe Gln Asn Ala Phe Ile Ser
50 55 60

Ser Val Pro Phe Gly Pro His Lys Ser Pro Trp Gly Val Gly Gly Gly
65 70 75 80

Leu Cys Arg His Pro His Phe Lys Ala Gly Ser
85 90

<210> 533
<211> 67
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (63)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 533
Asn Leu Cys Gln Val Gln Pro Thr Arg Leu Tyr Ser Ser Leu His Ser
1 5 10 15

Gly Leu His His Val Arg Gln Val Thr Gln Lys Ser Tyr Lys Val Ser
20 25 30

Thr Ser Gly Pro Arg Ala Phe Ser Ser Arg Ser Tyr Thr Ser Gly Pro
35 40 45

Gly Ser Arg Ile Ser Ser Ser Ala Phe Ser Arg Val Gly Gly Xaa Ser
50 55 60

Gly Gly Ala
65

<210> 534
<211> 144
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (140)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (141)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 534
Phe Asn Arg Arg Tyr Pro Lys Ile Gln Phe Ser Leu Ser Thr Gly Pro
1 5 10 15

Ser Gly Thr Met Leu Asp Gly Val Leu Glu Gly Lys Leu Asn Ala Ala
20 25 30

Phe Ile Asp Gly Pro Ile Asn His Thr Ala Ile Asp Gly Ile Pro Val
35 40 45

Tyr Arg Glu Glu Leu Met Ile Val Thr Pro Gln Gly Tyr Ala Pro Val
50 55 60

Thr Arg Ala Ser Gln Val Asn Gly Ser Asn Ile Tyr Ala Phe Arg Ala
65 70 75 80

Asn Cys Ser Tyr Arg Arg His Phe Glu Ser Trp Phe His Ala Asp Gly
85 90 95

Ala Ala Pro Gly Thr Ile His Glu Met Glu Ser Tyr His Gly Met Leu
100 105 110

Ala Cys Val Ile Ala Gly Ala Gly Ile Ala Leu Ile Pro Arg Ser Met
115 120 125

Leu Glu Ser Met Pro Gly His His Gln Val Glu Xaa Xaa Ala Val Ser
130 135 140

<210> 535
<211> 175
<212> PRT
<213> Homo sapiens

<400> 535
Arg Ala Pro Ala Arg Ile Ser Gly Gly Gly Ser Ala Met Val Gly Gly
1 5 10 15

Gly Gly Val Gly Gly Gly Leu Leu Glu Asn Ala Asn Pro Leu Ile Tyr
20 25 30

Gln Arg Ser Gly Glu Arg Pro Val Thr Ala Gly Glu Glu Asp Glu Gln
35 40 45

Val Pro Asp Ser Ile Asp Ala Arg Glu Ile Phe Asp Leu Ile Arg Ser
50 55 60

Ile Asn Asp Pro Glu His Pro Leu Thr Leu Glu Glu Leu Asn Val Val
65 70 75 80

Glu Gln Val Arg Val Gln Val Ser Asp Pro Glu Ser Thr Val Ala Val
85 90 95

Ala Phe Thr Pro Thr Ile Pro His Cys Ser Met Ala Thr Leu Ile Gly
100 105 110

Leu Ser Ile Lys Val Lys Leu Leu Arg Ser Leu Pro Gln Arg Phe Lys
115 120 125

Met Asp Val His Ile Thr Pro Gly Thr His Ala Ser Glu His Ala Val
130 135 140

Asn Lys Gln Leu Ala Asp Lys Glu Arg Val Ala Ala Ala Leu Glu Asn
145 150 155 160

Thr His Leu Leu Glu Val Val Asn Gln Cys Leu Ser Ala Arg Ser
165 170 175

<210> 536
<211> 148
<212> PRT
<213> Homo sapiens

<400> 536
Gly Trp His Arg Thr His His Arg Gly Arg His Gln Ala Arg Glu Ala
1   5   10   15

Glu Glu Glu Ala Trp Ala Ala Ala Glu Pro Ile Lys Lys Val Arg Lys
            20   25   30

Ser Leu Ala Leu Asp Ile Val Asp Glu Asp Val Lys Leu Met Met Ser
        35   40   45

Thr Leu Pro Lys Ser Leu Ser Leu Pro Thr Thr Ala Pro Ser Asn Ser
    50   55   60

Ser Ser Leu Thr Leu Ser Gly Ile Lys Glu Asp Asn Ser Leu Leu Asn
65   70   75   80

Gln Gly Phe Leu Gln Ala Lys Pro Glu Lys Ala Ala Val Ala Gln Lys
                85   90   95

Pro Arg Ser His Phe Thr Thr Pro Ala Pro Met Ser Ser Ala Trp Lys
            100   105   110

Thr Val Ala Cys Gly Gly Thr Arg Asp Gln Leu Phe Met Gln Glu Lys
        115   120   125

Ala Arg Gln Leu Leu Gly Arg Leu Lys Pro Ser His Thr Ser Arg Thr
    130   135   140

Leu Ile Leu Ser
145

<210> 537
<211> 70
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (42)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 537
Arg Pro Thr Arg Ser Ala Trp Trp Gly Arg Leu Leu Ser Arg Val Ser
1 5 10 15

Pro Gln Pro Arg Pro Ala Ser Pro Ser Val Ser Thr Arg Asn Gln Leu
20 25 30

Pro Glu Ala Arg Arg Gly Val Glu Xaa Xaa Glu Cys Glu Glu Thr Ala
35 40 45

Ala Ser Ala Glu Arg Ala Gly Pro Pro Arg Ala Leu Val Phe Gly Ala
50 55 60

Gln Ser Arg Ser Pro Gly
65 70

<210> 538
<211> 206
<212> PRT
<213> Homo sapiens

<400> 538
Gly Glu Val Ser Ala Ser Gly Ile Ala Arg Arg Gly Gly Pro Met Ala
1 5 10 15

Pro Leu Gly Gly Ala Pro Arg Leu Val Leu Leu Phe Ser Gly Lys Arg
20 25 30

Lys Ser Gly Lys Asp Phe Val Thr Glu Ala Leu Gln Ser Arg Leu Gly
35 40 45

Ala Asp Val Cys Ala Val Leu Arg Leu Ser Gly Pro Leu Lys Glu Gln
50 55 60

Tyr Ala Gln Glu His Gly Leu Asn Phe Gln Arg Leu Leu Asp Thr Ser
65 70 75 80

Thr Tyr Lys Glu Ala Phe Arg Lys Asp Met Ile Arg Trp Gly Glu Glu
85 90 95

Lys Arg Gln Ala Asp Pro Gly Phe Phe Cys Arg Lys Ile Val Glu Gly
100 105 110

Ile Ser Gln Pro Ile Trp Leu Val Ser Asp Thr Arg Arg Val Ser Asp
115 120 125

```
Ile Gln Trp Phe Arg Glu Ala Tyr Gly Ala Val Thr Gln Thr Val Arg
    130                 135                 140

Val Val Ala Leu Glu Gln Ser Arg Gln Gln Arg Gly Trp Val Phe Thr
145                 150                 155                 160

Pro Gly Val Asp Asp Ala Glu Ser Glu Cys Gly Leu Asp Asn Phe Gly
                165                 170                 175

Asp Phe Asp Trp Val Ile Glu Asn His Gly Val Glu Gln Arg Leu Glu
            180                 185                 190

Glu Gln Leu Glu Asn Leu Ile Glu Phe Ile Arg Ser Arg Leu
        195                 200                 205



<210> 539
<211> 350
<212> PRT
<213> Homo sapiens

<400> 539
Ser Thr Leu Ile Ala Phe Ile Val Ile Ser Thr Leu Phe Pro Leu Leu
  1               5                  10                  15

Asp Met Thr Glu Ile Tyr Phe Ser Leu Leu Asp Glu Ile Val Asp Thr
             20                  25                  30

Leu Gly Glu Gly Ala Phe Gly Lys Val Val Glu Cys Ile Asp His Lys
         35                  40                  45

Ala Gly Gly Arg His Val Ala Val Lys Ile Val Lys Asn Val Asp Arg
     50                  55                  60

Tyr Cys Glu Ala Ala Arg Ser Glu Ile Gln Val Leu Glu His Leu Asn
 65                  70                  75                  80

Thr Thr Asp Pro Asn Ser Thr Phe Arg Cys Val Gln Met Leu Glu Trp
                 85                  90                  95

Phe Glu His His Gly His Ile Cys Ile Val Phe Glu Leu Leu Gly Leu
            100                 105                 110

Ser Thr Tyr Asp Phe Ile Lys Glu Asn Gly Phe Leu Pro Phe Arg Leu
        115                 120                 125

Asp His Ile Arg Lys Met Ala Tyr Gln Ile Cys Lys Ser Val Asn Phe
    130                 135                 140
```

Leu His Ser Asn Lys Leu Thr His Thr Asp Leu Lys Pro Glu Asn Ile
145 150 155 160

Leu Phe Val Gln Ser Asp Tyr Thr Glu Ala Tyr Asn Pro Lys Ile Lys
165 170 175

Arg Asp Glu Arg Thr Leu Ile Asn Pro Asp Ile Lys Val Val Asp Phe
180 185 190

Gly Ser Ala Thr Tyr Asp Asp Glu His His Ser Thr Leu Val Ser Thr
195 200 205

Arg His Tyr Arg Ala Pro Glu Val Ile Leu Ala Leu Gly Trp Ser Gln
210 215 220

Pro Cys Asp Val Trp Ser Ile Gly Cys Ile Leu Ile Glu Tyr Tyr Leu
225 230 235 240

Gly Phe Thr Val Phe Pro Thr His Asp Ser Lys Glu His Leu Ala Met
245 250 255

Met Glu Arg Ile Leu Gly Pro Leu Pro Lys His Met Ile Gln Lys Thr
260 265 270

Arg Lys Arg Lys Tyr Phe His His Asp Arg Leu Asp Trp Asp Glu His
275 280 285

Ser Ser Ala Gly Arg Tyr Val Ser Arg Arg Cys Lys Pro Leu Lys Glu
290 295 300

Phe Met Leu Ser Gln Asp Val Glu His Glu Arg Leu Phe Asp Leu Ile
305 310 315 320

Gln Lys Met Leu Glu Tyr Asp Pro Ala Lys Arg Ile Thr Leu Arg Glu
325 330 335

Ala Leu Lys His Pro Phe Phe Asp Leu Leu Lys Lys Ser Ile
340 345 350

<210> 540
<211> 324
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (56)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (297)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (304)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (305)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (317)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (321)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 540

```
Gln Ala Thr Met Gly Asn Val Leu Ala Ala Ser Ser Pro Pro Ala Gly
  1               5                  10                  15

Pro Pro Pro Pro Pro Ala Pro Ala Leu Val Gly Leu Pro Pro Pro Pro
             20                  25                  30

Pro Ser Pro Pro Gly Phe Thr Leu Pro Pro Leu Gly Gly Ser Leu Gly
         35                  40                  45

Ala Gly Thr Ser Thr Xaa Arg Xaa Ser Glu Arg Thr Pro Gly Ala Ala
     50                  55                  60

Thr Ala Ser Ala Ser Gly Ala Ala Glu Asp Gly Ala Cys Gly Cys Leu
 65                  70                  75                  80

Pro Asn Pro Gly Thr Phe Glu Glu Cys His Arg Lys Cys Lys Glu Leu
                 85                  90                  95

Phe Pro Ile Gln Met Glu Gly Val Lys Leu Thr Val Asn Lys Gly Leu
            100                 105                 110
```

Ser Asn His Phe Gln Val Asn His Thr Val Ala Leu Ser Thr Ile Gly
        115   120   125

Glu Ser Asn Tyr His Phe Gly Val Thr Tyr Val Gly Thr Lys Gln Leu
    130   135   140

Ser Pro Thr Glu Ala Phe Pro Val Leu Val Gly Asp Met Asp Asn Ser
145   150   155   160

Gly Ser Leu Asn Ala Gln Val Ile His Gln Leu Gly Pro Gly Leu Arg
                165   170   175

Ser Lys Met Ala Ile Gln Thr Gln Gln Ser Lys Phe Val Asn Trp Gln
            180   185   190

Val Asp Gly Glu Tyr Arg Gly Ser Asp Phe Thr Ala Ala Val Thr Leu
        195   200   205

Gly Asn Pro Asp Val Leu Val Gly Ser Gly Ile Leu Val Ala His Tyr
    210   215   220

Leu Gln Ser Ile Thr Pro Cys Leu Ala Leu Gly Gly Glu Leu Val Tyr
225   230   235   240

His Arg Arg Pro Gly Glu Glu Gly Thr Val Met Ser Leu Ala Gly Lys
                245   250   255

Tyr Thr Leu Asn Asn Trp Leu Ala Thr Val Thr Leu Gly Gln Ala Gly
            260   265   270

Met His Ala Thr Tyr Tyr His Lys Ala Ser Asp Gln Leu Gln Val Gly
        275   280   285

Val Glu Phe Glu Ala Ser Thr Arg Xaa Gln Asp Thr Ser Val Ser Xaa
    290   295   300

Xaa Val Pro Ala Trp Asn Leu Pro Lys Gly Gln Pro Xaa Leu Ser Lys
305   310   315   320

Xaa Leu Leu Gly

<210> 541
<211> 204
<212> PRT
<213> Homo sapiens

<400> 541

Arg Gly Pro Thr Phe Thr Pro Glu Ile Met Ala Ala Glu Asp Val Val
1 5 10 15

Ala Thr Gly Ala Asp Pro Ser Asp Leu Glu Ser Gly Gly Leu Leu His
20 25 30

Glu Ile Phe Thr Ser Pro Leu Asn Leu Leu Leu Leu Gly Leu Cys Ile
35 40 45

Phe Leu Leu Tyr Lys Ile Val Arg Gly Asp Gln Pro Ala Ala Ser Gly
50 55 60

Asp Ser Asp Asp Asp Glu Pro Pro Pro Leu Pro Arg Leu Lys Arg Arg
65 70 75 80

Asp Phe Thr Pro Ala Glu Leu Arg Arg Phe Asp Gly Val Gln Asp Pro
85 90 95

Arg Ile Leu Met Ala Ile Asn Gly Lys Val Phe Asp Val Thr Lys Gly
100 105 110

Arg Lys Phe Tyr Gly Pro Glu Gly Pro Tyr Gly Val Phe Ala Gly Arg
115 120 125

Asp Ala Ser Arg Gly Leu Ala Thr Phe Cys Leu Asp Lys Glu Ala Leu
130 135 140

Lys Asp Glu Tyr Asp Asp Leu Ser Asp Leu Thr Ala Ala Gln Gln Glu
145 150 155 160

Thr Leu Ser Asp Trp Glu Ser Gln Phe Thr Phe Lys Tyr His His Val
165 170 175

Gly Lys Leu Leu Lys Glu Gly Glu Glu Pro Thr Val Tyr Ser Asp Glu
180 185 190

Glu Glu Pro Lys Asp Glu Ser Ala Arg Lys Asn Asp
195 200

<210> 542
<211> 193
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (183)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 542

```
Pro Ala Tyr Ser Leu Gly Leu Leu Lys Ser Val Leu Asp Gly Gly Gly
 1               5                  10                  15

Ala Gly Ala His Gln Ala Arg Ser Asn Pro Ser Cys Met Tyr Pro Gln
            20                  25                  30

Gly Thr Phe Val Ile Pro Leu Leu Val Thr Ala His Arg Asp Pro Thr
        35                  40                  45

Gln Phe Lys Asp Pro Asp Cys Phe Asn Pro Thr Asn Phe Leu Asp Lys
    50                  55                  60

Gly Lys Phe Gln Gly Asn Asp Ala Phe Met Pro Phe Ala Ser Gly Ala
65                  70                  75                  80

Gly Arg Gly Gly Arg Gly Pro Ala Trp Thr Gly Ser Gly Val Pro Gly
                85                  90                  95

Ala His Cys Ala Pro Val Tyr Pro Ala Lys Gln Met Cys Leu Gly Thr
            100                 105                 110

Gly Leu Ala His Ser Gly Ile Phe Leu Phe Leu Thr Ala Thr Leu Gln
        115                 120                 125

Arg Phe Cys Leu Leu Pro Val Val Arg Pro Gly Thr Ile Asn Leu Thr
    130                 135                 140

Cys Ser Ala Leu Ala Trp Ala Val Ser Pro Gln Thr Ser Ser Ser Ser
145                 150                 155                 160

Gln Trp Pro Ala Glu Val Arg Leu His Tyr Gly Gly Leu Thr Gly Pro
                165                 170                 175

Gln Thr Ser Ile Pro Ser Xaa Val Asn Lys Gly Pro Lys Leu Gln Lys
            180                 185                 190

Lys
```

<210> 543
<211> 352
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (154)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (167)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 543

```
Ser Thr Val Arg Xaa Pro Gly Arg Pro Thr Arg Pro Met Ala Ala Glu
  1               5                  10                  15

Glu Pro Gln Gln Gln Lys Gln Glu Pro Leu Gly Ser Asp Ser Glu Val
             20                  25                  30

Leu Thr Val Trp Pro Met Met Lys Pro Ser Trp Leu Ser Arg Thr Glu
         35                  40                  45

Phe Ser Lys Arg Leu Leu Cys Arg Thr Leu Trp Cys Gln Ser Gly Trp
     50                  55                  60

Ser Ser Arg Ser Tyr Thr Arg Ser Met Leu Lys Met Thr Thr Ser Ile
 65                  70                  75                  80

Asn Arg Arg Ser Arg Thr Ser Thr Lys Ser Thr Arg Thr Ser Ala Arg
                 85                  90                  95

Pro Gly Leu Thr Ala Thr Val Ser Ile Gly Leu Ser Asp Ser Pro Thr
            100                 105                 110

Trp Arg His Cys Trp Met Thr Ala Arg Ser Cys Ser Gly Glu Lys Gly
        115                 120                 125

Gly His Trp Ala Pro Arg Gln Val Gly Val Tyr Leu Leu Pro Gly Arg
    130                 135                 140

Val Gly Cys Val Ser Ser Arg Val Ser Xaa Ser Phe Pro Gly Asp Gly
145                 150                 155                 160

Leu Asp Ser Gly Leu Ala Xaa Arg Gly Ser Ala Val Ser Ala Leu Ala
                165                 170                 175

Ser Gly Leu Val Glu Glu Pro Met Leu Gly Pro Pro Phe His Pro Thr
            180                 185                 190

Pro Arg Phe Lys Ala Val Ser Ala Lys Ser Lys Glu Asp Leu Val Ser
        195                 200                 205
```

Gln Gly Phe Thr Glu Phe Thr Ile Glu Asp Phe His Asn Thr Phe Met
210 215 220

Asp Leu Ile Glu Gln Val Glu Lys Gln Thr Ser Val Ala Asp Leu Leu
225 230 235 240

Ala Ser Phe Asn Asp Gln Ser Thr Ser Asp Tyr Leu Val Val Tyr Leu
245 250 255

Arg Leu Leu Thr Ser Gly Tyr Leu Gln Arg Glu Ser Lys Phe Phe Glu
260 265 270

His Phe Ile Glu Gly Gly Arg Thr Val Lys Glu Phe Cys Gln Gln Glu
275 280 285

Val Glu Pro Met Cys Lys Glu Ser Asp His Ile His Ile Ile Ala Leu
290 295 300

Ala Gln Ala Leu Ser Val Ser Ile Gln Val Glu Tyr Met Asp Arg Gly
305 310 315 320

Glu Gly Gly Thr Thr Asn Pro His Ile Phe Pro Glu Gly Ser Glu Pro
325 330 335

Lys Val Tyr Leu Leu Tyr Arg Pro Gly His Tyr Asp Ile Leu Tyr Lys
340 345 350

<210> 544
<211> 240
<212> PRT
<213> Homo sapiens

<400> 544
Ser Thr His Ala Ser Glu Met Ala Glu Arg Gly Tyr Ser Phe Ser Leu
1 5 10 15

Thr Thr Phe Ser Pro Ser Gly Lys Leu Val Gln Ile Glu Tyr Ala Leu
20 25 30

Ala Ala Val Ala Gly Gly Ala Pro Ser Val Gly Ile Lys Ala Ala Asn
35 40 45

Gly Val Val Leu Ala Thr Glu Lys Lys Gln Lys Ser Ile Leu Tyr Asp
50 55 60

Glu Arg Ser Val His Lys Val Glu Pro Ile Thr Lys His Ile Gly Leu

65 70 75 80

Val Tyr Ser Gly Met Gly Pro Asp Tyr Arg Val Leu Val His Arg Ala
85 90 95

Arg Lys Leu Ala Gln Gln Tyr Tyr Leu Val Tyr Gln Glu Pro Ile Pro
100 105 110

Thr Ala Gln Leu Val Gln Arg Val Ala Ser Val Met Gln Glu Tyr Thr
115 120 125

Gln Ser Gly Gly Val Arg Pro Phe Gly Val Ser Leu Leu Ile Cys Gly
130 135 140

Trp Asn Glu Gly Arg Pro Tyr Leu Phe Gln Ser Asp Pro Ser Gly Ala
145 150 155 160

Tyr Phe Ala Trp Lys Ala Thr Ala Met Gly Lys Asn Tyr Val Asn Gly
165 170 175

Lys Thr Phe Leu Glu Lys Arg Tyr Asn Glu Asp Leu Glu Leu Glu Asp
180 185 190

Ala Ile His Thr Ala Ile Leu Thr Leu Lys Glu Ser Phe Glu Gly Gln
195 200 205

Met Thr Glu Asp Asn Ile Glu Val Gly Ile Cys Asn Glu Ala Gly Phe
210 215 220

Arg Arg Leu Thr Pro Thr Glu Val Lys Asp Tyr Leu Ala Ala Ile Ala
225 230 235 240

<210> 545
<211> 181
<212> PRT
<213> Homo sapiens

<400> 545
Arg Cys Ile Leu Tyr Thr Gly Phe Met Leu Gly Ala Gln Arg Glu Val
1 5 10 15

Asp Ser Arg Leu Leu Ala Leu Pro Gly Arg Lys Val Pro Thr Ser Trp
20 25 30

Trp Asp Asp Leu Phe Lys Gly Ala Lys Glu His Gly Ala Val Ala Val
35 40 45

Glu Arg Val Thr Lys Ser Pro Gly Glu Thr Ser Lys Pro Arg Pro Phe
50 55 60

Ala Gly Gly Gly Tyr Arg Leu Gly Ala Ala Pro Glu Glu Glu Ser Ala
65 70 75 80

Tyr Val Ala Gly Glu Lys Arg Gln His Ser Ser Gln Asp Val His Val
85 90 95

Val Leu Lys Leu Trp Lys Ser Gly Phe Ser Leu Asp Asn Gly Glu Leu
100 105 110

Arg Ser Tyr Gln Asp Pro Ser Asn Ala Gln Phe Leu Glu Ser Ile Arg
115 120 125

Arg Gly Glu Val Pro Ala Glu Leu Arg Arg Leu Ala His Gly Gly Gln
130 135 140

Val Asn Leu Asp Met Glu Asp His Arg Asp Glu Asp Phe Val Lys Pro
145 150 155 160

Lys Gly Ala Phe Lys Ala Phe Thr Gly Glu Gly Gln Lys Leu Gly Ser
165 170 175

Thr Ala Pro Arg Cys
180

<210> 546
<211> 197
<212> PRT
<213> Homo sapiens

<400> 546
Pro Arg Val Arg Arg Arg Ala Arg Ala Ala Ala Gly Ser Ser His Ala
1 5 10 15

Ala Met Ala Asp Ser Glu Leu Gln Leu Val Glu Gln Arg Ile Arg Ser
20 25 30

Phe Pro Asp Phe Pro Thr Pro Gly Val Val Phe Arg Asp Ile Ser Pro
35 40 45

Val Leu Lys Asp Pro Ala Ser Phe Arg Ala Ala Ile Gly Leu Leu Ala
50 55 60

Arg His Leu Lys Ala Thr His Gly Gly Arg Ile Asp Tyr Ile Ala Gly
65 70 75 80

```
Leu Asp Ser Arg Gly Phe Leu Phe Gly Pro Ser Leu Ala Gln Glu Leu
                 85                  90                  95

Gly Leu Gly Cys Val Leu Ile Arg Lys Arg Gly Lys Leu Pro Gly Pro
            100                 105                 110

Thr Leu Trp Ala Ser Tyr Ser Leu Glu Tyr Gly Lys Ala Glu Leu Glu
        115                 120                 125

Ile Gln Lys Asp Ala Leu Glu Pro Gly Gln Arg Val Val Val Val Asp
    130                 135                 140

Asp Leu Leu Ala Thr Gly Gly Thr Met Asn Ala Ala Cys Glu Leu Leu
145                 150                 155                 160

Gly Arg Leu Gln Ala Glu Val Leu Glu Cys Val Ser Leu Val Glu Leu
                165                 170                 175

Thr Ser Leu Lys Gly Arg Glu Lys Leu Ala Pro Val Pro Phe Phe Ser
            180                 185                 190

Leu Leu Gln Tyr Glu
        195
```

<210> 547
<211> 93
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 547

```
Glu Thr Gly Lys Glu Ser Lys Ala Leu Phe Leu Pro Phe Pro Gly Ser
  1               5                  10                  15

Val Tyr Ser Thr Ser Thr Gly Glu Ala Ser Gly Glu Gly Leu Ser Pro
             20                  25                  30

Leu Pro His Leu His Glu Phe Trp Asn Ser Val Leu Leu Ala Ala Cys
        35                  40                  45

Phe Gln Leu Pro Pro Ile Ser Ile Ala Ala Gly Ser Ser Cys Leu Phe
    50                  55                  60

Tyr Ser Val Ile Lys His Pro Ala Pro Thr Leu Ser Gln Arg Ser Ile
 65                  70                  75                  80
```

Leu Ile Leu Xaa Lys Lys Ile Tyr Glu Glu Lys Lys Lys
85 90

<210> 548
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 548
Gly Leu Gln Leu Xaa Ala His Ala Ala Gly Arg Val Pro Gly Cys Ala
1 5 10 15

Leu Gln Gly Leu Gly His Phe Leu Gln Glu Asn Lys Gln Leu Leu Arg
20 25 30

Asp Val Leu Ala Gln Glu Leu His Lys Pro Ala Phe Glu Gly Arg His
35 40 45

Ile

<210> 549
<211> 379
<212> PRT
<213> Homo sapiens

<400> 549
Val Ala Cys Cys Val Arg Ile Pro Gly Pro Pro Arg Arg Ser Gly Pro
1 5 10 15

Ala Met Ala Val Thr Ile Thr Leu Lys Thr Leu Gln Gln Gln Thr Phe
20 25 30

Lys Ile Arg Met Glu Pro Asp Glu Thr Val Lys Val Leu Lys Glu Lys
35 40 45

Ile Glu Ala Glu Lys Gly Arg Asp Ala Phe Pro Val Ala Gly Gln Lys
50 55 60

Leu Ile Tyr Ala Gly Lys Ile Leu Ser Asp Asp Val Pro Ile Arg Asp
65 70 75 80

```
Tyr Arg Ile Asp Glu Lys Asn Phe Val Val Val Met Val Thr Lys Thr
                85                  90                  95

Lys Ala Gly Gln Gly Thr Ser Ala Pro Pro Glu Ala Ser Pro Thr Ala
            100                 105                 110

Ala Pro Glu Ser Ser Thr Ser Phe Pro Pro Ala Pro Thr Ser Gly Met
        115                 120                 125

Ser His Pro Pro Pro Ala Ala Arg Glu Asp Lys Ser Pro Ser Glu Glu
    130                 135                 140

Ser Ala Pro Thr Thr Ser Pro Glu Ser Val Ser Gly Ser Val Pro Ser
145                 150                 155                 160

Ser Gly Ser Ser Gly Arg Glu Glu Asp Ala Ala Ser Thr Leu Val Thr
                165                 170                 175

Gly Ser Glu Tyr Glu Thr Met Leu Thr Glu Ile Met Ser Met Gly Tyr
            180                 185                 190

Glu Arg Glu Arg Val Val Ala Ala Leu Arg Ala Ser Tyr Asn Asn Pro
        195                 200                 205

His Arg Ala Val Glu Tyr Leu Leu Thr Gly Ile Pro Gly Ser Pro Glu
    210                 215                 220

Pro Glu His Gly Ser Val Gln Glu Ser Gln Val Ser Glu Gln Pro Ala
225                 230                 235                 240

Thr Glu Ala Gly Glu Asn Pro Leu Glu Phe Leu Arg Asp Gln Pro Gln
                245                 250                 255

Phe Gln Asn Met Arg Gln Val Ile Gln Gln Asn Pro Ala Leu Leu Pro
            260                 265                 270

Ala Leu Leu Gln Gln Leu Gly Gln Glu Asn Pro Gln Leu Leu Gln Gln
        275                 280                 285

Ile Ser Arg His Gln Glu Gln Phe Ile Gln Met Leu Asn Glu Pro Pro
    290                 295                 300

Gly Glu Leu Ala Asp Ile Ser Asp Val Glu Gly Glu Val Gly Ala Ile
305                 310                 315                 320

Gly Glu Glu Ala Pro Gln Met Asn Tyr Ile Gln Val Thr Pro Gln Glu
                325                 330                 335

Lys Glu Ala Ile Glu Arg Leu Lys Ala Leu Gly Phe Pro Glu Ser Leu
            340                 345                 350
```

Val Ile Gln Ala Tyr Phe Ala Cys Glu Lys Asn Glu Asn Leu Ala Ala
355 360 365

Asn Phe Leu Leu Ser Gln Asn Phe Asp Asp Glu
370 375

<210> 550
<211> 275
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (235)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (260)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (261)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (267)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (272)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 550
Cys Ser Cys Lys Arg Xaa His Gln Gln Gln Val Leu Pro Pro Arg Gln
1 5 10 15

Pro Ser Ala Leu Val Pro Ser Val Thr Glu Tyr Arg Leu Asp Gly His
20 25 30

Thr Ile Ser Asp Leu Ser Arg Ser Ser Arg Gly Glu Leu Ile Pro Ile
35 40 45

Ser Pro Ser Thr Glu Val Gly Gly Ser Gly Ile Gly Thr Pro Pro Ser
50 55 60

Val Leu Lys Arg Gln Arg Lys Arg Arg Val Ala Leu Ser Pro Val Thr
65 70 75 80

Glu Asn Ser Thr Ser Leu Ser Phe Leu Asp Ser Cys Asn Ser Leu Thr
85 90 95

Pro Lys Ser Thr Pro Val Lys Thr Leu Pro Phe Ser Pro Ser Gln Phe
100 105 110

Leu Asn Phe Trp Asn Lys Gln Asp Thr Leu Glu Leu Glu Ser Pro Ser
115 120 125

Leu Thr Ser Thr Pro Val Cys Ser Gln Lys Val Val Val Thr Thr Pro
130 135 140

Leu His Arg Asp Lys Thr Pro Leu His Gln Lys His Ala Ala Phe Val
145 150 155 160

Thr Pro Asp Gln Lys Tyr Ser Met Asp Asn Thr Pro His Thr Pro Thr
165 170 175

Pro Phe Lys Asn Ala Leu Glu Lys Tyr Gly Pro Leu Lys Pro Leu Pro
180 185 190

Gln Thr Pro His Leu Glu Glu Asp Leu Lys Glu Val Leu Arg Ser Glu
195 200 205

Ala Gly Ile Glu Leu Ile Ile Glu Asp Asp Ile Arg Pro Glu Lys Gln
210 215 220

Lys Arg Lys Pro Gly Leu Arg Arg Ser Pro Xaa Lys Lys Val Arg Lys
225 230 235 240

Ser Leu Ala Leu Asp Ile Val Asp Glu Asp Val Lys Leu Met Met Ser
245 250 255

Thr Leu Pro Xaa Xaa Leu Ser Leu Ala Thr Xaa Ala Pro Cys Lys Xaa
260 265 270

Phe Gln Pro
275

<210> 551

<211> 161
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (158)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 551

```
Asn Leu Ala Ala Ala Ser Gly Gly Gly Pro Gln Ser Val Ser Gly Thr
  1               5                  10                  15

Leu Leu Cys Glu Pro Val Leu Thr Met Phe Ala Thr Ser Gly Ala Val
             20                  25                  30

Ala Ala Gly Lys Pro Tyr Ser Cys Ser Glu Cys Gly Lys Ser Phe Cys
         35                  40                  45

Tyr Ser Ser Val Leu Leu Arg His Glu Arg Ala His Gly Gly Asp Gly
     50                  55                  60

Arg Phe Arg Cys Leu Glu Cys Gly Glu Arg Cys Ala Arg Ala Ala Asp
 65                  70                  75                  80

Leu Arg Ala His Arg Arg Thr His Ala Gly Gln Thr Leu Tyr Ile Cys
                 85                  90                  95

Ser Glu Cys Gly Gln Ser Phe Arg His Ser Gly Arg Leu Asp Leu His
            100                 105                 110

Leu Gly Ala His Arg Gln Arg Cys Arg Thr Cys Pro Cys Arg Thr Cys
        115                 120                 125

Gly Arg Arg Phe Pro His Leu Pro Ala Leu Leu Leu His Arg Arg Arg
    130                 135                 140

Gln His Leu Pro Glu Arg Pro Arg Arg Cys Pro Leu Cys Xaa Leu Arg
145                 150                 155                 160

Phe
```

<210> 552
<211> 405
<212> PRT
<213> Homo sapiens

<400> 552

Pro Arg Val Arg Arg Arg Ala Arg Gly Arg Arg Val Arg Pro Ala Gly
1   5   10   15

Gly Pro Val Arg Arg Gly Ala Ala Val Arg Gly Ala Leu Arg Gly Ala
            20   25   30

Ser Leu Gly His Gly Ala Ala Ala Arg Ala Gly Arg Pro Leu Cys Val
        35   40   45

Arg His Ser Glu Pro Val Cys Gly Ser Asp Ala Asn Thr Tyr Ala Asn
    50   55   60

Leu Cys Gln Leu Arg Ala Ala Ser Arg Arg Ser Glu Arg Leu His Arg
65   70   75   80

Pro Pro Val Ile Val Leu Gln Arg Gly Ala Cys Gly Gln Gly Gln Glu
                85   90   95

Asp Pro Asn Ser Leu Arg His Lys Tyr Asn Phe Ile Ala Asp Val Val
            100   105   110

Glu Lys Ile Ala Pro Ala Val Val His Ile Glu Leu Phe Arg Lys Leu
        115   120   125

Pro Phe Ser Lys Arg Glu Val Pro Val Ala Ser Gly Ser Gly Phe Ile
    130   135   140

Val Ser Glu Asp Gly Leu Ile Val Thr Asn Ala His Val Val Thr Asn
145   150   155   160

Lys His Arg Val Lys Val Glu Leu Lys Asn Gly Ala Thr Tyr Glu Ala
                165   170   175

Lys Ile Lys Asp Val Asp Glu Lys Ala Asp Ile Ala Leu Ile Lys Ile
            180   185   190

Asp His Gln Gly Lys Leu Pro Val Leu Leu Leu Gly Arg Ser Ser Glu
        195   200   205

Leu Arg Pro Gly Glu Phe Val Val Ala Ile Gly Ser Pro Phe Ser Leu
    210   215   220

Gln Asn Thr Val Thr Thr Gly Ile Val Ser Thr Thr Gln Arg Gly Gly
225   230   235   240

Lys Glu Leu Gly Leu Arg Asn Ser Asp Met Asp Tyr Ile Gln Thr Asp
                245   250   255

Ala Ile Ile Asn Tyr Gly Asn Ser Gly Gly Pro Leu Val Asn Leu Asp
            260   265   270

Gly Glu Val Ile Gly Ile Asn Thr Leu Lys Val Thr Ala Gly Ile Ser
275 280 285

Phe Ala Ile Pro Ser Asp Lys Ile Lys Lys Phe Leu Thr Glu Ser His
290 295 300

Asp Arg Gln Ala Lys Gly Lys Ala Ile Thr Lys Lys Lys Tyr Ile Gly
305 310 315 320

Ile Arg Met Met Ser Leu Thr Ser Ser Lys Ala Lys Glu Leu Lys Asp
325 330 335

Arg His Arg Asp Phe Pro Asp Val Ile Ser Gly Ala Tyr Ile Ile Glu
340 345 350

Val Ile Pro Asp Thr Pro Ala Glu Ala Gly Gly Leu Lys Glu Asn Asp
355 360 365

Val Ile Ile Ser Ile Asn Gly Gln Ser Val Val Ser Ala Asn Asp Val
370 375 380

Ser Asp Val Ile Lys Arg Glu Ser Thr Leu Asn Met Val Val Arg Arg
385 390 395 400

Val Met Lys Ile Ser
405

<210> 553
<211> 107
<212> PRT
<213> Homo sapiens

<400> 553
Ala Gln Glu Asn Glu Glu Met Glu Gln Pro Met Gln Asn Gly Glu Glu
1 5 10 15

Asp Arg Pro Leu Gly Gly Gly Glu Gly His Gln Pro Ala Gly Asn Arg
20 25 30

Arg Gly Gln Ala Arg Arg Leu Ala Pro Asn Phe Arg Trp Ala Ile Pro
35 40 45

Asn Arg Gln Ile Asn Asp Gly Met Gly Gly Asp Gly Asp Asp Met Glu
50 55 60

Ile Phe Met Glu Glu Met Arg Glu Ile Arg Arg Lys Leu Arg Glu Leu
65 70 75 80

Gln Leu Arg Asn Cys Leu Arg Ile Leu Met Gly Glu Leu Ser Asn His

85 90 95

His Asp His His Asp Glu Phe Cys Leu Met Pro
100 105

<210> 554
<211> 229
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (20)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (27)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 554
Gly Leu Ser Ala Glu Ser Thr Xaa Thr Ser Thr Met Pro Met Xaa Leu
1 5 10 15

Gly Tyr Trp Xaa Ile Arg Gly Leu Ala His Xaa Ile Arg Leu Leu Leu
20 25 30

Glu Tyr Thr Asp Ser Ser Tyr Glu Glu Lys Lys Tyr Thr Met Gly Asp
35 40 45

Ala Pro Asp Tyr Asp Arg Ser Gln Trp Leu Asn Glu Lys Phe Lys Leu
50 55 60

Gly Leu Asp Phe Pro Asn Leu Pro Tyr Leu Ile Asp Gly Xaa His Lys

65 70 75 80

Ile Thr Gln Ser Asn Ala Ile Leu Arg Tyr Ile Ala Arg Lys His Asn
85 90 95

Leu Cys Gly Glu Ser Glu Lys Glu Gln Ile Arg Glu Asp Ile Leu Glu
100 105 110

Asn Gln Phe Met Asp Ser Arg Met Gln Leu Ala Lys Leu Cys Tyr Asp
115 120 125

Pro Asp Phe Glu Lys Leu Lys Pro Glu Tyr Leu Gln Ala Leu Pro Glu
130 135 140

Met Leu Lys Leu Tyr Ser Gln Phe Leu Gly Lys Gln Pro Trp Phe Leu
145 150 155 160

Gly Asp Lys Ile Thr Phe Val Asp Phe Ile Ala Tyr Asp Val Leu Glu
165 170 175

Arg Asn Gln Val Phe Glu Pro Ser Cys Leu Asp Ala Phe Pro Asn Leu
180 185 190

Lys Asp Phe Ile Ser Arg Phe Glu Gly Leu Glu Lys Ile Ser Ala Tyr
195 200 205

Met Lys Ser Ser Arg Phe Leu Pro Arg Pro Val Phe Thr Lys Met Ala
210 215 220

Val Trp Gly Asn Lys
225

<210> 555
<211> 106
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (60)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (72)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (98)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 555
Asn Val Ile Ser Val Asp Pro Asn Asp Gln Lys Lys Thr Ala Cys Tyr
1 5 10 15

Asp Ile Asp Val Glu Val Asp Asp Thr Leu Lys Thr Gln Met Asn Ser
20 25 30

Phe Leu Leu Ser Thr Ala Ser Gln Gln Glu Ile Ala Thr Leu Asp Asn
35 40 45

Lys Thr Met Thr Asp Val Val Gly Asn Gln Xaa Xaa Ser Ala Glu Leu
50 55 60

Ser Ser Thr Ser Ser Pro Gly Xaa Gly Gly Cys Val Pro Ile Leu Leu
65 70 75 80

Leu Gln Gly Ala Ala Glu Thr Thr Arg Ile Arg Ala Ser Pro Gly Asn
85 90 95

Pro Xaa Tyr Ile Gly Pro Leu Pro Gln Pro
100 105

<210> 556
<211> 86
<212> PRT
<213> Homo sapiens

<400> 556
Gly Arg Ala Thr Lys Gln Asn Thr Thr Lys Pro Asn His Arg Ile Ile
1 5 10 15

Phe Asn Pro Thr Phe Tyr Thr Met Pro Gln Phe Pro Ile Thr Leu His
20 25 30

Thr Ser Phe Cys Val Gln Leu Asn Cys Asn Cys Phe Leu Tyr Leu Glu
35 40 45

Arg Val Thr Ile Glu Leu Glu Thr Phe Tyr Ser Gly Arg Leu Gly Ser
50 55 60

Phe Trp Trp Asp Ser Val Gly Glu Arg Glu Glu Gly Glu Val Gly Gly

65 70 75 80

Leu Leu Pro Phe Arg Thr
85

<210> 557
<211> 565
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (57)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (71)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (75)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (82)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (118)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (120)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (552)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 557
Ala Ser Leu Thr Gly Thr Gln Ala Leu Pro Pro Leu Phe Ser Leu Gly
1 5 10 15

```
Tyr His Gln Ser Arg Trp Asn Tyr Arg Asp Glu Ala Asp Val Leu Glu
            20                  25                  30

Val Asp Gln Gly Phe Asp Asp His Asn Leu Pro Cys Asp Val Ile Trp
        35                  40                  45

Leu Asp Ile Glu His Ala Asp Gly Xaa Arg Tyr Phe Thr Trp Asp Pro
    50                  55                  60

Ser Arg Phe Pro Gln Pro Xaa Thr Met Leu Xaa Arg Leu Ala Ser Lys
65                  70                  75                  80

Arg Xaa Lys Leu Val Ala Ile Val Asp Pro His Ile Lys Val Asp Ser
                85                  90                  95

Gly Tyr Arg Val His Glu Glu Leu Arg Asn Leu Gly Leu Tyr Val Lys
            100                 105                 110

Thr Arg Asp Gly Ser Xaa Tyr Xaa Gly Trp Cys Trp Pro Gly Ser Ala
        115                 120                 125

Gly Tyr Pro Asp Phe Thr Asn Pro Thr Met Arg Ala Trp Trp Ala Asn
    130                 135                 140

Met Phe Ser Tyr Asp Asn Tyr Glu Gly Ser Ala Pro Asn Leu Phe Val
145                 150                 155                 160

Trp Asn Asp Met Asn Glu Pro Ser Val Phe Asn Gly Pro Glu Val Thr
                165                 170                 175

Met Leu Lys Asp Ala Gln His Tyr Gly Gly Trp Glu His Arg Asp Val
            180                 185                 190

His Asn Ile Tyr Gly Leu Tyr Val His Met Ala Thr Ala Asp Gly Leu
        195                 200                 205

Arg Gln Arg Ser Gly Gly Met Glu Arg Pro Phe Val Leu Ala Arg Ala
    210                 215                 220

Phe Phe Ala Gly Ser Gln Arg Phe Gly Ala Val Trp Thr Gly Asp Asn
225                 230                 235                 240

Thr Ala Glu Trp Asp His Leu Lys Ile Ser Ile Pro Met Cys Leu Ser
                245                 250                 255

Leu Gly Leu Val Gly Leu Ser Phe Cys Gly Ala Asp Val Gly Gly Phe
            260                 265                 270

Phe Lys Asn Pro Glu Pro Glu Leu Leu Val Arg Trp Tyr Gln Met Gly
        275                 280                 285
```

Ala Tyr Gln Pro Phe Phe Arg Ala His Ala His Leu Asp Thr Gly Arg
290 295 300

Arg Glu Pro Trp Leu Leu Pro Ser Gln His Asn Asp Ile Ile Arg Asp
305 310 315 320

Ala Leu Gly Gln Arg Tyr Ser Leu Leu Pro Phe Trp Tyr Thr Leu Leu
325 330 335

Tyr Gln Ala His Arg Glu Gly Ile Pro Val Met Arg Pro Leu Trp Val
340 345 350

Gln Tyr Pro Gln Asp Val Thr Thr Phe Asn Ile Asp Asp Gln Tyr Leu
355 360 365

Leu Gly Asp Ala Leu Leu Val His Pro Val Ser Asp Ser Gly Ala His
370 375 380

Gly Val Gln Val Tyr Leu Pro Gly Gln Gly Glu Val Trp Tyr Asp Ile
385 390 395 400

Gln Ser Tyr Gln Lys His His Gly Pro Gln Thr Leu Tyr Leu Pro Val
405 410 415

Thr Leu Ser Ser Ile Pro Val Phe Gln Arg Gly Gly Thr Ile Val Pro
420 425 430

Arg Trp Met Arg Val Arg Arg Ser Ser Glu Cys Met Lys Asp Asp Pro
435 440 445

Ile Thr Leu Phe Val Ala Leu Ser Pro Gln Gly Thr Ala Gln Gly Glu
450 455 460

Leu Phe Leu Asp Asp Gly His Thr Phe Asn Tyr Gln Thr Arg Gln Glu
465 470 475 480

Phe Leu Leu Arg Arg Phe Ser Phe Ser Gly Asn Thr Leu Val Ser Ser
485 490 495

Ser Ala Asp Pro Glu Gly His Phe Glu Thr Pro Ile Trp Ile Glu Arg
500 505 510

Val Val Ile Ile Gly Ala Gly Lys Pro Ala Ala Val Val Leu Gln Thr
515 520 525

Lys Gly Ser Pro Glu Ser Arg Leu Ser Phe Gln His Asp Pro Glu Thr
530 535 540

Ser Val Leu Val Leu Arg Lys Xaa Gly Ile Asn Val Ala Ser Asp Trp
545 550 555 560

```
Ser Ile His Leu Arg
                565



<210> 558
<211> 160
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (39)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 558
Arg Glu Ala Val Leu Pro Gln Ala Val Leu Arg His Pro Val Arg Thr
  1               5                  10                  15

Gln Arg Arg Glu His Arg Gly Arg Gly Leu Leu His Leu Arg Glu Ala
             20                  25                  30

Pro Gly Gly Gly Ala Ala Xaa His Arg Pro His Arg Gly Pro Arg Gly
         35                  40                  45

Pro Ser Arg Gly Ala Glu Gly Glu Arg Pro Pro Glu Gly Pro Ser Arg
     50                  55                  60

Ala Ser Ser Val Thr Thr Phe Thr Gly Glu Pro Asn Thr Cys Pro Arg
 65                  70                  75                  80

Cys Ser Lys Lys Val Tyr Phe Ala Glu Lys Val Thr Ser Leu Gly Lys
                 85                  90                  95

Asp Trp His Arg Pro Cys Leu Arg Cys Glu Arg Cys Gly Lys Thr Leu
            100                 105                 110

Thr Pro Gly Gly His Ala Glu His Asp Gly Gln Pro Tyr Cys His Lys
        115                 120                 125

Pro Cys Tyr Gly Ile Leu Phe Gly Pro Lys Gly Val Asn Thr Gly Ala
    130                 135                 140

Val Gly Ser Tyr Ile Tyr Asp Arg Asp Pro Glu Gly Lys Val Gln Pro
145                 150                 155                 160
```

<210> 559
<211> 480
<212> PRT
<213> Homo sapiens

<400> 559
Gly Cys Ile Gly Tyr Leu Val Leu Leu Trp Pro Leu Pro Leu Ile His
1 5 10 15

Phe Gly Leu Ala Asn Gln Ser Glu Asp Leu Ser Val Phe Tyr Pro Gly
20 25 30

Thr Leu Leu Glu Thr Gly His Asp Ile Leu Phe Phe Trp Val Ala Arg
35 40 45

Met Val Met Leu Gly Leu Lys Leu Thr Gly Arg Leu Pro Phe Arg Glu
50 55 60

Val Tyr Leu His Ala Ile Val Arg Asp Ala His Gly Arg Lys Met Ser
65 70 75 80

Lys Ser Leu Gly Asn Val Ile Asp Pro Leu Asp Val Ile Tyr Gly Ile
85 90 95

Ser Leu Gln Gly Leu His Asn Gln Leu Leu Asn Ser Asn Leu Asp Pro
100 105 110

Ser Glu Val Glu Lys Ala Lys Glu Gly Gln Lys Ala Asp Phe Pro Ala
115 120 125

Gly Ile Pro Glu Cys Gly Thr Asp Ala Leu Arg Phe Gly Leu Cys Ala
130 135 140

Tyr Met Ser Gln Gly Arg Asp Ile Asn Leu Asp Val Asn Arg Ile Leu
145 150 155 160

Gly Tyr Arg His Phe Cys Asn Lys Leu Trp Asn Ala Thr Lys Phe Ala
165 170 175

Leu Arg Gly Leu Gly Lys Gly Phe Val Pro Ser Pro Thr Ser Gln Pro
180 185 190

Gly Gly His Glu Ser Leu Val Asp Arg Trp Ile Arg Ser Arg Leu Thr
195 200 205

Glu Ala Val Arg Leu Ser Asn Gln Gly Phe Gln Ala Tyr Asp Phe Pro
210 215 220

Ala Val Thr Thr Ala Gln Tyr Ser Phe Trp Leu Tyr Glu Leu Cys Asp
225 230 235 240

Val Tyr Leu Glu Cys Leu Lys Pro Val Leu Asn Gly Val Asp Gln Val
245 250 255

Ala Ala Glu Cys Ala Arg Gln Thr Leu Tyr Thr Cys Leu Asp Val Gly
260 265 270

Leu Arg Leu Leu Ser Pro Phe Met Pro Phe Val Thr Glu Glu Leu Phe
275 280 285

Gln Arg Leu Pro Arg Arg Met Pro Gln Ala Pro Pro Ser Leu Cys Val
290 295 300

Thr Pro Tyr Pro Glu Pro Ser Glu Cys Ser Trp Lys Asp Pro Glu Ala
305 310 315 320

Glu Ala Ala Leu Glu Leu Ala Leu Ser Ile Thr Arg Ala Val Arg Ser
325 330 335

Leu Arg Ala Asp Tyr Asn Leu Thr Arg Ile Arg Pro Asp Cys Phe Leu
340 345 350

Glu Val Ala Asp Glu Ala Thr Gly Ala Leu Ala Ser Ala Val Ser Gly
355 360 365

Tyr Val Gln Ala Leu Ala Ser Ala Gly Val Val Ala Val Leu Ala Leu
370 375 380

Gly Ala Pro Ala Pro Gln Gly Cys Ala Val Ala Leu Ala Ser Asp Arg
385 390 395 400

Cys Ser Ile His Leu Gln Leu Gln Gly Leu Val Asp Pro Ala Arg Glu
405 410 415

Leu Gly Lys Leu Gln Ala Lys Arg Val Glu Ala Gln Arg Gln Ala Gln
420 425 430

Arg Leu Arg Glu Arg Arg Ala Ala Ser Gly Tyr Pro Val Lys Val Pro
435 440 445

Leu Glu Val Gln Glu Ala Asp Glu Ala Lys Leu Gln Gln Thr Glu Ala
450 455 460

Glu Leu Arg Lys Val Asp Glu Ala Ile Ala Leu Phe Gln Lys Met Leu
465 470 475 480

<210> 560

<211> 96
<212> PRT
<213> Homo sapiens

<400> 560
Ala Cys Leu Glu Arg Cys Gly Ser Trp Arg Pro His Arg Pro Met Thr
1 5 10 15

Ser Gly Ala Arg Glu Asn Pro Ile Gln Val Pro Arg Ser Ser Leu Glu
20 25 30

Ala Thr Gly Ala Gln Glu Arg Trp Ala Glu Asp Val Pro Tyr Pro Thr
35 40 45

Thr Arg Ala Val Ser Leu Pro Pro Ser Leu Gly Val Gly Ser Thr Gly
50 55 60

Met Ser Ser Ser Arg Phe Leu Gly Ser Leu Gly Lys His Gly Arg Leu
65 70 75 80

Asp Ser Ser Arg Arg Ala Arg Leu Trp Gly Arg Gly Gly Arg Gly Gly
85 90 95

<210> 561
<211> 60
<212> PRT
<213> Homo sapiens

<400> 561
Ile Arg His Glu Ser Ser Ile Leu Ser Val Leu Phe Ile Arg Phe Leu
1 5 10 15

Lys Cys Ala Asp Pro Phe Lys Thr Pro Ala Tyr Leu Cys Asn Lys Glu
20 25 30

Lys Tyr Ser Lys Ile Leu Pro Ser Phe Ser His Thr Val Leu Lys Met
35 40 45

Leu Gln Asp Gln Ile Ile Ala His Lys Ile Arg Ser
50 55 60

<210> 562
<211> 241
<212> PRT

<213> Homo sapiens

<400> 562

Ser Ser Met Ala Lys Pro Cys Gly Val Arg Leu Ser Gly Glu Ala Arg
1 5 10 15

Lys Gln Val Glu Val Phe Arg Gln Asn Leu Phe Gln Glu Ala Glu Glu
20 25 30

Phe Leu Tyr Arg Phe Leu Pro Gln Lys Ile Ile Tyr Leu Asn Gln Leu
35 40 45

Leu Gln Glu Asp Ser Leu Asn Val Ala Asp Leu Thr Ser Leu Arg Ala
50 55 60

Pro Leu Asp Ile Pro Ile Pro Asp Pro Pro Pro Lys Asp Asp Glu Met
65 70 75 80

Glu Thr Asp Lys Gln Glu Lys Lys Glu Val Pro Lys Cys Gly Phe Leu
85 90 95

Pro Gly Asn Glu Lys Val Leu Ser Leu Leu Ala Leu Val Lys Pro Glu
100 105 110

Val Trp Thr Leu Lys Glu Lys Cys Ile Leu Val Ile Thr Trp Ile Gln
115 120 125

His Leu Ile Pro Lys Ile Glu Asp Gly Asn Asp Phe Gly Val Ala Ile
130 135 140

Gln Glu Lys Val Leu Glu Arg Val Asn Ala Val Lys Thr Lys Val Glu
145 150 155 160

Ala Phe Gln Thr Thr Ile Ser Lys Tyr Phe Ser Glu Arg Gly Asp Ala
165 170 175

Val Ala Lys Ala Ser Lys Glu Thr His Val Met Asp Tyr Arg Ala Leu
180 185 190

Val His Glu Arg Asp Glu Ala Ala Tyr Gly Glu Leu Arg Ala Met Val
195 200 205

Leu Asp Leu Arg Ala Phe Tyr Ala Glu Leu Tyr His Ile Ile Ser Ser
210 215 220

Asn Leu Glu Lys Ile Val Asn Pro Lys Gly Glu Glu Lys Pro Ser Met
225 230 235 240

Tyr

<210> 563
<211> 200
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (145)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 563
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Leu Gly Ser Ile Gln Val Met Gln Ala Val Arg Asn Ala Gly Ser Arg
  1               5                  10                  15

Phe Leu Arg Ser Trp Thr Trp Pro Gln Thr Ala Gly Arg Val Val Ala
             20                  25                  30

Arg Thr Pro Ala Gly Thr Ile Cys Thr Gly Ala Arg Gln Leu Gln Asp
         35                  40                  45

Ala Ala Ala Lys Gln Lys Val Glu Gln Asn Ala Ala Pro Ser His Thr
     50                  55                  60

Lys Phe Ser Ile Tyr Pro Pro Ile Pro Gly Glu Glu Ser Ser Leu Arg
 65                  70                  75                  80

Trp Ala Gly Lys Lys Phe Glu Glu Ile Pro Ile Ala His Ile Lys Ala
                 85                  90                  95

Ser His Asn Asn Thr Gln Ile Gln Val Val Ser Ala Ser Asn Glu Pro
            100                 105                 110

Leu Ala Phe Ala Ser Cys Gly Thr Glu Gly Phe Arg Asn Ala Lys Lys
        115                 120                 125

Gly Thr Gly Ile Ala Ala Gln Thr Ala Gly Ile Ala Ala Ala Ala Arg
    130                 135                 140

Xaa Lys Gln Lys Gly Val Ile His Ile Arg Val Val Val Lys Gly Leu
145                 150                 155                 160

Gly Pro Gly Arg Leu Ser Ala Met His Gly Leu Ile Met Gly Gly Leu
                165                 170                 175

Glu Val Ile Ser Ile Thr Asp Asn Thr Pro Ile Pro His Asn Gly Cys
            180                 185                 190

Arg Pro Arg Lys Ala Arg Lys Leu
        195                 200
```

<210> 564
<211> 115
<212> PRT
<213> Homo sapiens

<400> 564
Val Arg Leu Val Pro Gly Ala Asp Lys Tyr Asn Asp Asp Ile Arg Lys
1 5 10 15

Gly Ile Val Leu Leu Glu Glu Leu Leu Pro Lys Gly Ser Lys Glu Glu
20 25 30

Gln Arg Asp Tyr Val Phe Tyr Leu Ala Val Gly Asn Tyr Arg Leu Lys
35 40 45

Glu Tyr Glu Lys Ala Leu Lys Tyr Val Arg Gly Leu Leu Gln Thr Glu
50 55 60

Pro Gln Asn Asn Gln Ala Lys Glu Leu Glu Arg Leu Ile Asp Lys Ala
65 70 75 80

Met Lys Lys Asp Gly Leu Val Gly Met Ala Ile Val Gly Gly Met Ala
85 90 95

Leu Gly Val Ala Gly Leu Ala Gly Leu Ile Gly Leu Ala Val Ser Lys
100 105 110

Ser Lys Ser
115

<210> 565
<211> 101
<212> PRT
<213> Homo sapiens

<400> 565
Pro Thr Arg Pro Asp Glu His Asp Glu Asn Asn Ala Glu Ala Ser Ala
1 5 10 15

Glu Leu Ser Asn Glu Gly Val Met Asn His Arg Ser Glu Glu Glu Arg
20 25 30

Val Thr Glu Thr Gln Lys Asn Glu Arg Val Lys Lys Gln Leu Gln Ala
35 40 45

Leu Ser Ser Glu Leu Ala Gln Ala Arg Asp Glu Thr Lys Lys Thr Gln

50 55 60

Asn Asp Val Leu His Ala Glu Asn Val Lys Ala Gly Arg Asp Lys Tyr
65 70 75 80

Lys Thr Leu Arg Gln Ile Arg Gln Gly Asn Thr Lys Gln Arg Ile Asp
85 90 95

Glu Phe Glu Ala Met
100

<210> 566
<211> 25
<212> PRT
<213> Homo sapiens

<400> 566
Thr Ala Asp Leu Val Ile Arg Pro Pro Arg Pro Leu Lys Val Leu Gly
1 5 10 15

Phe Cys Val Phe Cys Ala Pro Pro Leu
20 25

<210> 567
<211> 274
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (182)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (216)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (222)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (224)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (228)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (231)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 567

```
Ala Ser Pro Glu Val Glu Ala Gly Ala Ala Arg Gln Pro Leu Leu Gly
  1               5                  10                  15

Val Ala Gly Gly Gln Thr Leu Gly Ala Thr Pro Gly Pro Val Met Asn
             20                  25                  30

Gly Pro Ala Asp Gly Glu Val Asp Tyr Lys Lys Lys Tyr Arg Asn Leu
         35                  40                  45

Lys Arg Lys Leu Lys Phe Leu Ile Tyr Glu His Glu Cys Phe Gln Glu
     50                  55                  60

Glu Leu Arg Lys Ala Gln Arg Lys Leu Leu Lys Val Ser Arg Asp Lys
 65                  70                  75                  80

Ser Phe Leu Leu Asp Arg Leu Leu Gln Tyr Glu Asn Val Asp Glu Asp
                 85                  90                  95

Ser Ser Asp Ser Asp Ala Thr Ala Ser Ser Asp Asn Ser Glu Thr Glu
            100                 105                 110

Gly Thr Pro Lys Leu Ser Asp Thr Pro Ala Pro Lys Arg Lys Arg Ser
        115                 120                 125

Pro Pro Leu Gly Gly Ala Pro Ser Pro Ser Ser Leu Ser Leu Pro Pro
    130                 135                 140

Ser Thr Gly Phe Pro Leu Gln Ala Ser Gly Val Pro Ser Pro Tyr Leu
145                 150                 155                 160

Ser Ser Leu Ala Ser Ser Arg Tyr Pro Pro Phe Pro Ser Asp Tyr Leu
                165                 170                 175

Ala Leu Gln Leu Pro Xaa Pro Ser Pro Leu Arg Pro Lys Arg Glu Lys
            180                 185                 190

Arg Pro Arg Leu Pro Arg Lys Leu Lys Met Ala Val Gly Pro Pro Asp
        195                 200                 205
```

Cys Pro Val Gly Gly Pro Leu Xaa Phe Pro Gly Arg Gly Xaa Gly Xaa
    210   215   220

Gly Val Gly Xaa Thr Leu Xaa Pro Leu Pro Pro Pro Lys Met Pro Pro
225   230   235   240

Pro Thr Ile Leu Ser Thr Val Pro Arg Gln Met Phe Ser Asp Ala Gly
                245   250   255

Ser Gly Asp Asp Ala Leu Asp Gly Asp Asp Asp Leu Val Ile Asp Ile
            260   265   270

Pro Glu

<210> 568
<211> 133
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (47)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 568
Ala Arg Gly Asp His Val Arg Ser Arg Glu Thr Gly Arg Gln Ser Ala
  1   5   10   15

Ser Lys Gly Gln Ile Pro Leu Leu Pro Arg Gly Pro Ala Val Pro Gly
             20   25   30

Gly Pro Ser Ala Gln Thr Ala Ala Gln Arg Glu Leu Arg Gly Xaa Val
         35   40   45

Gly Ala Gly Ala Pro Val Tyr Leu Ala Ala Val Leu Glu Tyr Leu Thr
     50   55   60

Ala Glu Ile Leu Glu Leu Ala Gly Asn Ala Ala Arg Asp Asn Lys Lys
 65   70   75   80

Thr Arg Ile Ile Pro Arg His Leu Gln Leu Ala Ile Arg Asn Asp Glu
                 85   90   95

Glu Leu Asn Lys Leu Leu Gly Lys Val Thr Ile Ala Gln Gly Gly Val
            100   105   110

Leu Pro Asn Ile Gln Ala Val Leu Leu Pro Lys Lys Thr Glu Ser Gln
        115   120   125

Lys Thr Lys Ser Lys
    130

<210> 569
<211> 153
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (136)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (137)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (152)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 569
Met Cys Arg Gly Tyr Ala Trp Asn Pro Gly Ile Thr Leu Gln Asn Arg
1   5   10   15

Lys Thr Lys Glu Gly Pro Arg Ala Pro Pro Ser Arg Met Pro Glu Pro
            20   25   30

Ala Gly Gly Leu Arg Gly Cys Glu Ala Val Gly Thr Leu Leu Met Lys
        35   40   45

Glu Thr Val Phe Ala Leu His Pro Ser Leu Pro Leu Gly Ala Gly Ser
    50   55   60

Ser Pro Ser Ala Thr Cys Ser Glu Gly Leu His Leu Arg Gly Glu Gly
65   70   75   80

Trp Gly Lys Ser Pro Pro Val Pro Phe Leu Trp Pro Cys Cys Pro His
                85   90   95

Thr Gln Leu Arg Gly Pro Thr Leu Gly Lys Ala Gly Ser Ala Arg Ser
            100   105   110

Leu Ser Pro Ile Ser Ala Leu Ser Ala Trp Ile Pro Ala Glu Ala Met
        115   120   125

Lys Gly Asn Lys Glu Lys Arg Xaa Xaa Lys Lys Lys Lys Lys Lys Lys
130 135 140

Lys Lys Lys Lys Lys Lys Lys Xaa Pro
145 150

<210> 570
<211> 327
<212> PRT
<213> Homo sapiens

<400> 570
Pro Gly Ser Pro Arg Arg Cys Asp Ile Ile Ile Ile Ser Gly Arg Lys
1 5 10 15

Glu Lys Cys Glu Ala Ala Lys Glu Ala Leu Glu Ala Leu Val Pro Val
20 25 30

Thr Ile Glu Val Glu Val Pro Phe Asp Leu His Arg Tyr Val Ile Gly
35 40 45

Gln Lys Gly Ser Gly Ile Arg Lys Met Met Asp Glu Phe Glu Val Asn
50 55 60

Ile His Val Pro Ala Pro Glu Leu Gln Ser Asp Ile Ile Ala Ile Thr
65 70 75 80

Gly Leu Ala Ala Asn Leu Asp Arg Ala Lys Ala Gly Leu Leu Glu Arg
85 90 95

Val Lys Glu Leu Gln Ala Glu Gln Glu Asp Arg Ala Leu Arg Ser Phe
100 105 110

Lys Leu Ser Val Thr Val Asp Pro Lys Tyr His Pro Lys Ile Ile Gly
115 120 125

Arg Lys Gly Ala Val Ile Thr Gln Ile Arg Leu Glu His Asp Val Asn
130 135 140

Ile Gln Phe Pro Asp Lys Asp Asp Gly Asn Gln Pro Gln Asp Gln Ile
145 150 155 160

Thr Ile Thr Gly Tyr Glu Lys Asn Thr Glu Ala Ala Arg Asp Ala Ile
165 170 175

Leu Arg Ile Val Gly Glu Leu Glu Gln Met Val Ser Glu Asp Val Pro
180 185 190

Leu Asp His Arg Val His Ala Arg Ile Ile Gly Ala Arg Gly Lys Ala

195 200 205

Ile Arg Lys Ile Met Asp Glu Phe Lys Val Asp Ile Arg Phe Pro Gln
210 215 220

Ser Gly Ala Pro Asp Pro Asn Cys Val Thr Val Thr Gly Leu Pro Glu
225 230 235 240

Asn Val Glu Glu Ala Ile Asp His Ile Leu Asn Leu Glu Glu Glu Tyr
245 250 255

Leu Ala Asp Val Val Asp Ser Glu Ala Leu Gln Val Tyr Met Lys Pro
260 265 270

Pro Ala His Glu Glu Ala Lys Ala Pro Ser Arg Gly Phe Val Val Arg
275 280 285

Asp Ala Pro Trp Thr Ala Ser Ser Ser Glu Lys Ala Pro Asp Met Ser
290 295 300

Ser Ser Glu Glu Phe Pro Ser Phe Gly Ala Gln Val Ala Pro Lys Thr
305 310 315 320

Leu Pro Trp Gly Pro Lys Arg
325

<210> 571
<211> 166
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 571
Gly Asn Ser Arg Val Asp Pro Arg Xaa Arg Gly Xaa Ala His Thr Cys
1 5 10 15

Ala Pro Cys Pro Ala Pro Gly Pro Leu Ala Gly Arg Ala Val Ser Gly
20 25 30

His Gly Ser Leu Pro Pro Asp Arg Arg Ala Pro Ser Ala Leu Ser Ser

35 40 45

Pro Ala Asp Glu Gly Glu Arg Arg Arg Pro Asp Leu Asp Glu Ile His
50 55 60

Arg Glu Leu Arg Pro Gln Gly Ser Ala Arg Pro Gln Pro Asp Pro Asn
65 70 75 80

Ala Glu Phe Asp Pro Asp Leu Pro Gly Gly Gly Leu His Arg Cys Leu
85 90 95

Ala Cys Ala Arg Tyr Phe Ile Asp Ser Thr Asn Leu Lys Thr His Phe
100 105 110

Arg Ser Lys Asp His Lys Lys Arg Leu Lys Gln Leu Ser Val Glu Pro
115 120 125

Tyr Ser Gln Glu Glu Ala Glu Arg Ala Ala Gly Met Gly Ser Tyr Val
130 135 140

Pro Pro Arg Arg Leu Ala Val Pro Thr Glu Val Ser Thr Glu Val Pro
145 150 155 160

Glu Met Asp Thr Ser Thr
165

<210> 572
<211> 113
<212> PRT
<213> Homo sapiens

<400> 572
Gln Ser Ser Thr Phe His Pro Ala Pro Ala Phe Gly Ala Thr Val Ala
1 5 10 15

Ala Phe His Arg Arg Ala Ala Leu Arg Ala Pro Glu Pro Ala Met Ser
20 25 30

Gly Pro Asn Gly Asp Leu Gly Met Pro Val Glu Ala Gly Ala Glu Gly
35 40 45

Glu Glu Asp Gly Phe Gly Glu Ala Glu Tyr Ala Ala Ile Asn Ser Met
50 55 60

Leu Asp Gln Ile Asn Ser Cys Leu Asp His Leu Glu Glu Lys Asn Asp
65 70 75 80

His Leu His Ala Arg Leu Gln Glu Leu Leu Glu Ser Asn Arg Gln Thr
85 90 95

Arg Leu Glu Phe Gln Gln Gln Leu Gly Glu Ala Pro Ser Asp Ala Ser
100 105 110

Pro

<210> 573
<211> 99
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (27)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (37)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 573
Gly Ser Gly Ser Ser Arg Asp Leu His Lys Ala Leu Trp Glu Ala Gly
1 5 10 15

Trp Glu Thr Val Glu Gly Gly Cys Pro Leu Xaa Pro Arg Arg His Arg
20 25 30

Ile Trp Ala Leu Xaa Xaa Ala Phe Leu Pro Glu Tyr Ala Ala Ile Asn
35 40 45

Ser Met Leu Asp Gln Ile Asn Ser Cys Leu Asp His Leu Glu Glu Lys
50 55 60

Asn Asp His Leu His Ala Arg Leu Gln Glu Leu Leu Glu Ser Asn Arg
65 70 75 80

Gln Thr Arg Leu Glu Phe Gln Gln Gln Leu Gly Glu Ala Pro Ser Asp
85 90 95

Ala Ser Pro

<210> 574
<211> 197
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (97)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (129)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 574
Arg Trp Ala Arg Val Glu Ala Ala Val Met Glu Gly Ala Gly Ala Gly
1 5 10 15

Ser Gly Phe Arg Lys Glu Leu Val Ser Arg Leu Leu His Leu His Phe
20 25 30

Lys Asp Asp Lys Thr Lys Val Ser Gly Asp Ala Leu Gln Leu Met Val
35 40 45

Glu Leu Leu Lys Val Phe Val Val Glu Ala Ala Val Arg Gly Val Arg
50 55 60

Gln Ala Gln Ala Glu Asp Ala Leu Arg Val Asp Val Asp Gln Leu Glu
65 70 75 80

Lys Val Leu Arg Ser Cys Ser Gly Leu Leu Gly Ile Ser Ala Val Ala
85 90 95

Xaa Ala Thr Pro Arg Gly Ala Pro Gly Pro Gln Lys Gln Ala Leu Cys
100 105 110

Phe Gln Arg Pro Leu Ile Arg Gly Arg Glu Gly Xaa Glu Gly Phe Gly
115 120 125

Xaa Asp Ser Asn Lys Ile Ser Gly Ser Leu Gln Pro Val Gln Lys Gly
130 135 140

Gln Asp Cys Ser Ala Leu Arg Ala Leu Glu Cys Pro Val Gly Thr Leu

145 150 155 160

Val Trp Glu Gly Ala Ala Pro Gly Glu Ser Leu Pro Leu Leu Pro Gly
165 170 175

Thr Ile Val Cys Met Pro Pro Gly Val Leu Gln Ala Gly Ala Gly Lys
180 185 190

Gly Leu Ala Ser Arg
195

<210> 575
<211> 47
<212> PRT
<213> Homo sapiens

<400> 575
Leu Pro Met Val Asp Leu Met Glu Lys Leu Asn Ile Phe His Tyr Ala
1 5 10 15

Leu Gln Asn Thr Val Tyr Val Ser Ala Ser Leu Gly Asn Gly Arg Gly
20 25 30

Gln Lys Lys Val Thr Phe Asn Leu Cys Ile Phe Ala Lys Pro Tyr
35 40 45

<210> 576
<211> 115
<212> PRT
<213> Homo sapiens

<400> 576
Trp Ser Arg Thr Ser Gln Pro Leu Pro Ser Thr Val Gly Cys Pro Arg
1 5 10 15

Arg Arg Gly Phe Lys Asp Phe Gln Arg Arg Ile Leu Val Ala Thr Asn
20 25 30

Leu Phe Gly Arg Gly Met Asp Ile Glu Arg Val Asn Ile Ala Phe Asn
35 40 45

Tyr Asp Met Pro Glu Asp Ser Asp Thr Tyr Leu His Arg Val Ala Arg
50 55 60

Ala Gly Arg Phe Gly Thr Lys Gly Leu Ala Ile Thr Phe Val Ser Asp
65 70 75 80

Glu Asn Asp Ala Lys Ile Leu Asn Asp Val Gln Asp Arg Phe Glu Val
85 90 95

Asn Ile Ser Glu Leu Pro Asp Glu Ile Asp Ile Ser Ser Tyr Ile Glu
100 105 110

Gln Thr Arg
115

<210> 577
<211> 346
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (37)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 577
Val Thr Ser Cys Val Ala Leu Leu Pro Ala Arg Arg Met Thr Tyr Thr
1 5 10 15

Thr Glu Thr Ala Leu Leu Asn Trp Ser Thr Cys Gln Met Val Leu Arg
20 25 30

Gly Ala Glu Thr Xaa Gly Cys Val Ile Val Ser Ala Ala Lys Ala Gln
35 40 45

Leu Leu Gln Cys Gln His His Pro Ala Trp Tyr Gly Asp Thr Leu Lys
50 55 60

Gln Lys Thr Ser Trp Thr Cys Leu Leu Asp Gly Met Gln Tyr Phe Ala
65 70 75 80

Thr Thr Glu Ser Ser Pro Thr Glu Gln Asp Gly Arg Gln Leu Trp Leu
85 90 95

Glu Val Lys Asn Ile Glu Glu His Arg Gln Arg Ser Leu Asp Ser Val
100 105 110

Gln Glu Leu Met Glu Ser Gly Gln Ala Val Gly Gly Met Val Thr Thr
115 120 125

Thr Thr Asp Trp Asn Gln Pro Ala Glu Ala Gln Gln Ala Gln Gln Val
130 135 140

Gln Arg Ile Ile Ser Arg Cys Asn Cys Arg Met Tyr Tyr Ile Ser Tyr
145 150 155 160

Ser His Asp Ile Asp Pro Glu Leu Ala Thr Gln Ile Lys Pro Pro Glu
165 170 175

Val Leu Glu Asn Gln Glu Lys Glu Asp Leu Leu Lys Lys Gln Glu Gly
180 185 190

Ala Val Asp Thr Phe Thr Leu Ile His His Glu Leu Glu Ile Ser Thr
195 200 205

Asn Pro Ala Gln Tyr Ala Met Ile Leu Asp Ile Val Asn Asn Leu Leu
210 215 220

Leu His Val Glu Pro Lys Arg Lys Glu His Ser Glu Lys Lys Gln Arg
225 230 235 240

Val Arg Phe Gln Leu Glu Ile Ser Ser Asn Pro Glu Glu Gln Arg Ser
245 250 255

Ser Ile Leu His Leu Gln Glu Ala Val Arg Gln His Val Ala Gln Ile
260 265 270

Arg Gln Leu Glu Lys Gln Met Tyr Ser Ile Met Lys Ser Leu Gln Asp
275 280 285

Asp Ser Lys Asn Glu Asn Leu Leu Asp Leu Asn Gln Lys Leu Gln Leu
290 295 300

Gln Leu Asn Gln Glu Lys Ala Asn Leu Gln Leu Glu Ser Glu Glu Leu
305 310 315 320

Asn Ile Leu Ile Arg Cys Phe Lys Asp Phe Gln Leu Gln Arg Ala Asn
325 330 335

Lys Met Glu Leu Arg Lys His Lys Lys Met
340 345

<210> 578
<211> 91
<212> PRT
<213> Homo sapiens

<400> 578
Arg His Glu Gly His Leu Gly Ser Gly Arg Asn Gly Gly Gly Ser Met
1 5 10 15

Asn Ala Pro Pro Ala Phe Glu Ser Phe Leu Leu Phe Glu Gly Glu Lys
20 25 30

Ile Thr Ile Asn Lys Asp Thr Lys Val Pro Asn Ala Cys Leu Phe Thr
35 40 45

Ile Asn Lys Glu Asp His Thr Leu Gly Asn Ile Ile Lys Ser Arg Ala
50 55 60

Cys Phe Pro Phe Ala Phe Cys Arg Asp Cys Gln Phe Pro Glu Ala Ser
65 70 75 80

Pro Ala Thr Leu Pro Val Gln Pro Ala Glu Leu
85 90

<210> 579
<211> 331
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (20)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (300)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (311)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (313)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (320)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (325)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 579
Gly Arg Pro Thr Arg Pro Gly Gly Leu Gly Ser Gly Val Leu Ala Leu
1 5 10 15

Ala Xaa Gly Xaa Pro Ala Arg Leu Ala Gly Thr Val His Glu Val Gly
20 25 30

Asp Ala Pro Arg Arg Ala Pro Asp Gln Ala Ala Glu Ile Gly Ser Arg
35 40 45

Gly Ser Thr Lys Ala Gln Gly Pro Gln Gln Gln Pro Gly Ser Glu Gly
50 55 60

Pro Ser Tyr Ala Lys Lys Val Ala Leu Trp Leu Ala Gly Leu Leu Gly
65 70 75 80

Ala Gly Gly Thr Val Ser Val Val Tyr Ile Phe Gly Asn Asn Pro Val
85 90 95

Asp Glu Asn Gly Ala Lys Ile Pro Asp Glu Phe Asp Asn Asp Pro Ile
100 105 110

Leu Val Gln Gln Leu Arg Arg Thr Tyr Lys Tyr Phe Lys Asp Tyr Arg
115 120 125

Gln Met Ile Ile Glu Pro Thr Ser Pro Cys Leu Leu Pro Asp Pro Leu
130 135 140

Gln Glu Pro Tyr Tyr Gln Pro Pro Tyr Thr Leu Val Leu Glu Leu Thr
145 150 155 160

Gly Val Leu Leu His Pro Glu Trp Ser Leu Ala Thr Gly Trp Arg Phe
165 170 175

Lys Lys Arg Pro Gly Ile Glu Thr Leu Phe Gln Gln Leu Ala Pro Leu
180 185 190

Tyr Glu Ile Val Ile Phe Thr Ser Glu Thr Gly Met Thr Ala Phe Pro
195 200 205

Leu Ile Asp Ser Val Asp Pro His Gly Phe Ile Ser Tyr Arg Leu Phe
210 215 220

Arg Asp Ala Thr Arg Tyr Met Asp Gly His His Val Lys Asp Ile Ser
225 230 235 240

Cys Leu Asn Arg Asp Pro Ala Arg Val Val Val Val Asp Cys Lys Lys
245 250 255

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Glu Ala Phe Arg Leu Gln Pro Tyr Asn Gly Val Ala Leu Arg Pro Trp
            260                 265                 270

Asp Gly Asn Ser Asp Asp Arg Val Leu Leu Asp Leu Ser Ala Phe Leu
        275                 280                 285

Lys Thr Ile Ala Leu Asn Gly Val Gly Gly Arg Xaa Glu Pro Cys Trp
    290                 295                 300

Glu His Tyr Ala Leu Gly Xaa Asp Xaa Pro Arg Trp Ala Ala Phe Xaa
305                 310                 315                 320

Asn Ser Gly Lys Xaa Gly Leu Glu Ala Gly Arg
                325                 330
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<210> 580
<211> 374
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (235)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (285)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (307)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (319)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (324)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (341)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (359)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 580
Pro Ser Thr Val Arg Asn Ser Arg Val Asp Pro Arg Val Arg Pro Arg
1   5   10   15

Val Arg Ala Gly Val Ala Ala Leu Ala Thr Val Gly Val Ala Ser Gly
            20   25   30

Pro Gly Pro Gly Arg Pro Gly Pro Leu Gln Asp Glu Thr Leu Gly Val
        35   40   45

Ala Ser Val Pro Ser Gln Trp Arg Ala Val Gln Gly Ile Arg Gly Glu
    50   55   60

Thr Lys Ser Cys Gln Thr Ala Ser Ile Ala Thr Ala Ser Ala Ser Ala
65   70   75   80

Gln Ala Arg Asn His Val Asp Ala Gln Val Gln Thr Glu Ala Pro Val
                85   90   95

Pro Val Ser Val Gln Pro Pro Ser Gln Tyr Asp Ile Pro Arg Leu Ala
            100   105   110

Ala Phe Leu Arg Arg Val Glu Ala Met Val Ile Arg Glu Leu Asn Lys
        115   120   125

Asn Trp Gln Ser His Ala Phe Asp Gly Phe Glu Val Asn Trp Thr Glu
    130   135   140

Gln Gln Gln Met Val Ser Cys Leu Tyr Thr Leu Gly Tyr Pro Pro Ala
145   150   155   160

Gln Ala Gln Gly Leu His Val Thr Ser Ile Ser Trp Asn Ser Thr Gly
                165   170   175

Ser Val Val Ala Cys Ala Tyr Gly Arg Leu Asp His Gly Asp Trp Ser
            180   185   190

Thr Leu Lys Ser Phe Val Cys Ala Trp Asn Leu Asp Arg Arg Asp Leu
        195   200   205

Arg Pro Gln Gln Pro Ser Ala Val Val Glu Val Pro Ser Ala Val Leu
    210   215   220

Cys Leu Ala Phe His Pro Thr Gln Pro Ser Xaa Val Ala Gly Gly Leu

225 230 235 240

Tyr Ser Gly Glu Val Leu Val Trp Asp Leu Ser Arg Leu Glu Asp Pro
245 250 255

Leu Leu Trp Arg Thr Gly Leu Thr Asp Asp Thr His Thr Asp Pro Val
260 265 270

Ser Gln Val Val Trp Leu Pro Glu Pro Gly His Ser Xaa Arg Phe Gln
275 280 285

Val Leu Ser Val Ala Thr Asp Gly Lys Val Leu Leu Trp Gln Gly Ile
290 295 300

Gly Val Xaa Gln Leu Gln Phe Thr Glu Gly Phe Ala Trp Phe Xaa Gln
305 310 315 320

Gln Leu Pro Xaa Ser Thr Lys Leu Lys Lys His Pro Arg Gly Arg Pro
325 330 335

Arg Trp Ala Pro Xaa Gln Ala Phe Phe Gln Phe Asp Leu Arg Phe Ser
340 345 350

Phe Trp Gln Glu Ala Val Xaa Val Gln Phe Ser Trp His Trp Arg Ala
355 360 365

Ala Leu Arg Gly Ala His
370

<210> 581
<211> 94
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (80)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 581
Cys Pro Asp Gln Asn Gly Trp Ala Ser Phe Gly Ala Pro Leu Ser Ala
1 5 10 15

Gly Gly Gln Pro Cys Tyr Leu Leu Asp Ile Gly Cys Gly Ser Gly Leu

20 25 30

Ser Gly Asp Tyr Leu Ser Asp Glu Gly His Tyr Trp Val Gly Ile Asp
35 40 45

Ile Ser Pro Ala Met Leu Asp Ala Ala Leu Asp Arg Asp Thr Glu Gly
50 55 60

Asp Leu Leu Leu Gly Asp Met Gly Gln Gly Ile Pro Phe Lys Pro Xaa
65 70 75 80

Ser Leu Met Asp Val Ser Ala Phe Cys Xaa Ser Val Ala Leu
85 90

<210> 582
<211> 163
<212> PRT
<213> Homo sapiens

<400> 582
Pro Thr Arg Pro Ala Ala Gly Gly Ala Glu Arg Ile Ala Gly Ser Ala
1 5 10 15

Met Ser Ser Glu Pro Pro Pro Pro Pro Gln Pro Pro Thr His Gln Ala
20 25 30

Ser Val Gly Leu Leu Asp Thr Pro Arg Ser Arg Glu Arg Ser Pro Ser
35 40 45

Pro Leu Arg Gly Asn Val Val Pro Ser Pro Leu Pro Thr Arg Arg Thr
50 55 60

Arg Thr Phe Ser Ala Thr Val Arg Ala Ser Gln Gly Pro Val Tyr Lys
65 70 75 80

Gly Val Cys Lys Cys Phe Cys Arg Ser Lys Gly His Gly Phe Ile Thr
85 90 95

Pro Ala Asp Gly Gly Pro Asp Ile Phe Leu His Ile Ser Asp Val Glu
100 105 110

Gly Glu Tyr Val Pro Val Glu Gly Asp Glu Val Thr Tyr Lys Met Cys
115 120 125

Ser Ile Pro Pro Lys Asn Glu Lys Leu Gln Ala Val Glu Val Val Ile
130 135 140

Thr His Leu Ala Pro Gly Thr Lys His Glu Thr Trp Ser Gly His Val
145 150 155 160

Ile Ser Ser

<210> 583
<211> 293
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (52)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (53)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (58)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (150)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (171)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (207)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (254)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 583
Leu Leu Gly Pro Asn Leu Thr Met Gly Ser Gln Pro Gly Arg Ile Pro
1 5 10 15

Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr

20 25 30

Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met Ile Asp Ser Glu
35 40 45

Cys Arg Pro Xaa Xaa Arg Glu Leu Val Xaa Glu Phe Ser Arg Met Ala
50 55 60

Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu Asp Leu Gly Pro
65 70 75 80

Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp
85 90 95

Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu Val Pro Gln Gln
100 105 110

Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly Gly Met Val His
115 120 125

His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly Gly Asp Leu Thr
130 135 140

Leu Gly Leu Glu Pro Xaa Glu Arg Gly Gly Pro Gln Val Ser Thr Gly
145 150 155 160

Thr Leu Arg Arg Ala Gly Ser Asp Val Phe Xaa Gly Asp Leu Gly Met
165 170 175

Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His Asp Pro Ser Pro
180 185 190

Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu Pro Ser Xaa Thr
195 200 205

Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val
210 215 220

Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro
225 230 235 240

Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Xaa Lys Thr
245 250 255

Leu Ser Pro Gly Lys Asn Gly Val Val Lys Glu Phe Leu Pro Leu Gly
260 265 270

Val Pro Trp Arg Thr Pro Ser Ile Asp Thr Pro Gly Glu Gly Ala Cys
275 280 285

Pro Ser Ala Pro Pro

290

<210> 584
<211> 132
<212> PRT
<213> Homo sapiens

<400> 584
Gly Gly Ala Gln Pro Gly Met Glu Gly Ala Ala Ala Thr Val His Leu
1 5 10 15

Ile Ser Gln Trp Ala Val Glu Pro Asn Ala Arg Val Gly Pro Leu Leu
20 25 30

Glu Val Glu Ala Ala Ala Ala Asp His His Glu Ala Ala Ala Gly Ala
35 40 45

Gly Ser Ala Val Glu Lys Ile Cys Ile Asp Lys Gly Leu Thr Asp Glu
50 55 60

Ser Glu Ile Leu Arg Phe Leu Gln His Gly Thr Leu Val Gly Leu Leu
65 70 75 80

Pro Val Pro His Pro Ile Leu Ile Arg Lys Tyr Gln Ala Asn Ser Gly
85 90 95

Thr Ala Met Trp Phe Arg Thr Tyr Met Trp Gly Val Ile Tyr Leu Arg
100 105 110

Asn Val Asp Pro Pro Val Trp Tyr Asp Thr Asp Val Lys Leu Phe Glu
115 120 125

Ile Gln Arg Val
130

<210> 585
<211> 218
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (92)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (117)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (140)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (141)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (188)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (199)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (200)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 585
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Arg Glu Arg Cys Arg Arg Glu Ala Leu Arg Gly Ser Arg Leu Cys Pro
  1               5                  10                  15

Ala Thr Pro Pro Ser Ala Leu Gly Ser Gln Asp Gly Ser Arg Thr Arg
             20                  25                  30

Asp Arg Leu Gly Ala Ala Gly Trp Pro Gly Leu Val Val Gly Leu Cys
         35                  40                  45

Thr Pro Ala Ala Gly Xaa Gln Arg Asp Leu Leu His Arg Arg Gly Gly
     50                  55                  60

Thr Ala Ser Phe Gly Lys Ser Phe Ala Gln Lys Ser Gly Tyr Phe Leu
 65                  70                  75                  80

Cys Leu Ser Ser Leu Gly Ser Leu Glu Asn Pro Xaa Glu Asn Val Val
                 85                  90                  95
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Ala Asp Ile Gln Ile Val Val Asp Lys Ser Pro Leu Pro Leu Gly Phe
        100                 105                 110

Ser Pro Val Cys Xaa Pro Met Asp Ser Lys Ala Ser Val Ser Lys Lys
    115                 120                 125

Lys Arg Met Cys Val Lys Leu Leu Pro Leu Gly Xaa Xaa Asp Thr Ala
130                 135                 140

Val Phe Asp Val Arg Leu Ser Gly Lys Thr Lys Thr Val Pro Gly Tyr
145                 150                 155                 160

Leu Arg Ile Gly Asp Met Gly Gly Phe Ala Ile Trp Cys Lys Lys Gly
                165                 170                 175

Gln Gly Pro Glu Ala Ser Cys Pro Lys Pro Arg Xaa Pro Gln Pro Gly
            180                 185                 190

Thr Cys Lys Gly Phe Ser Xaa Xaa Ala Ala Ser Gln Pro Lys Leu Arg
        195                 200                 205

Ala Gly Leu Leu Gly Ser Arg Thr Ser Val
    210                 215


<210> 586
<211> 233
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 586
Ala Arg Gly Glu Met Glu Gly Arg Gln Val Leu Glu Val Lys Met Gln
1               5                   10                  15

Val Glu Tyr Met Ser Phe Ser Ala His Ala Asp Ala Lys Gly Ile Met
            20                  25                  30

Gln Leu Val Gly Gln Ala Glu Pro Xaa Ser Val Leu Leu Val His Gly
        35                  40                  45

Glu Ala Lys Lys Met Glu Phe Leu Lys Gln Lys Ile Glu Gln Glu Leu
    50                  55                  60

Arg Val Asn Cys Tyr Met Pro Ala Asn Gly Glu Thr Val Thr Leu Pro
```

65 70 75 80

Thr Ser Pro Ser Ile Pro Val Gly Ile Ser Leu Gly Leu Leu Lys Arg
85 90 95

Glu Met Ala Gln Gly Leu Leu Pro Glu Ala Lys Lys Pro Arg Leu Leu
100 105 110

His Gly Thr Leu Ile Met Lys Asp Ser Asn Phe Arg Leu Val Ser Ser
115 120 125

Glu Gln Ala Leu Lys Glu Leu Gly Leu Ala Glu His Gln Leu Arg Phe
130 135 140

Thr Cys Arg Val His Leu His Asp Thr Arg Lys Glu Gln Glu Thr Ala
145 150 155 160

Leu Arg Val Tyr Ser His Leu Lys Ser Val Leu Lys Asp His Cys Val
165 170 175

Gln His Leu Pro Asp Gly Ser Val Thr Val Glu Ser Val Leu Leu Gln
180 185 190

Ala Ala Ala Pro Ser Glu Asp Pro Gly Thr Lys Val Leu Leu Val Ser
195 200 205

Trp Thr Tyr Gln Asp Glu Glu Leu Gly Ser Phe Leu Thr Ser Leu Leu
210 215 220

Lys Lys Gly Leu Pro Gln Ala Pro Ser
225 230

<210> 587
<211> 116
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (100)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 587
Gly Pro Leu Ser His His Ile Arg Ala Gln Leu Ser Lys Met Leu Leu
1 5 10 15

Ala Arg Lys Gln Ile Leu Cys Val Asn Val Lys Asn Phe Ala Val Ile
20 25 30

Tyr Leu Val Asp Ile Thr Glu Val Pro Asp Phe Asn Lys Met Tyr Glu
35 40 45

Leu Tyr Asp Pro Cys Thr Val Met Phe Phe Phe Arg Asn Lys His Ile
50 55 60

Met Ile Asp Leu Gly Thr Gly Asn Asn Asn Lys Ile Asn Trp Ala Met
65 70 75 80

Glu Asp Lys Gln Glu Met Val Asp Ile Ile Glu Thr Val Tyr Arg Gly
85 90 95

Ala Arg Lys Xaa Arg Gly Leu Val Val Ser Pro Lys Asp Tyr Ser Thr
100 105 110

Lys Tyr Arg Tyr
115

<210> 588
<211> 133
<212> PRT
<213> Homo sapiens

<400> 588
Ala Arg Ala Ala Val Gly Arg Thr Ala Gly Val Arg Thr Trp Ala Pro
1 5 10 15

Leu Ala Met Ala Ala Lys Val Asp Leu Ser Thr Ser Thr Asp Trp Lys
20 25 30

Glu Ala Lys Ser Phe Leu Lys Gly Leu Ser Asp Lys Gln Arg Glu Glu
35 40 45

His Tyr Phe Cys Lys Asp Phe Val Arg Leu Lys Lys Ile Pro Thr Trp
50 55 60

Lys Glu Met Ala Lys Gly Val Ala Val Lys Val Glu Glu Pro Arg Tyr
65 70 75 80

Lys Lys Asp Lys Gln Leu Asn Glu Lys Ile Ser Leu Leu Arg Ser Asp
85 90 95

Ile Thr Lys Leu Glu Val Asp Ala Ile Val Asn Ala Ala Asn Ser Ser
100 105 110

Pro Pro Pro Arg Ser Leu Ile Lys Asp Leu Arg Cys Gly Lys Lys Lys
115 120 125

Lys Lys Lys Lys Lys

130

<210> 589
<211> 163
<212> PRT
<213> Homo sapiens

<400> 589
Arg His Arg Gly Gln Pro Leu Arg Gln Thr Arg Ala Ser Ser Ser Pro
1   5   10   15

Gln Leu Ala Gly Arg Ser Ser Ser Val Leu Pro Ala Ala Ala Gln Pro
            20   25   30

Cys Thr Pro Thr Met Asp Val Phe Lys Lys Gly Phe Ser Ile Ala Lys
        35   40   45

Glu Gly Val Val Gly Ala Val Glu Lys Thr Lys Gln Gly Val Thr Glu
    50   55   60

Ala Ala Glu Lys Thr Lys Glu Gly Val Met Tyr Val Gly Ala Lys Thr
65   70   75   80

Lys Glu Asn Val Val Gln Ser Val Thr Ser Val Ala Glu Lys Thr Lys
                85   90   95

Glu Gln Ala Asn Ala Val Ser Glu Ala Val Val Ser Ser Val Asn Thr
            100   105   110

Val Ala Thr Lys Thr Val Glu Glu Ala Glu Asn Ile Ala Val Thr Ser
        115   120   125

Gly Val Val Arg Lys Glu Asp Leu Arg Pro Ser Ala Pro Gln Gln Glu
    130   135   140

Gly Glu Ala Ser Lys Glu Lys Glu Glu Val Ala Glu Glu Ala Gln Ser
145   150   155   160

Gly Gly Asp

<210> 590
<211> 59
<212> PRT
<213> Homo sapiens

<400> 590

```
Arg Ala Leu Leu Cys Leu Gly His His Pro Leu Leu Ala Gln Gly Val
  1               5                  10                  15

Pro Ala Leu Ser Asp Met Arg Leu Pro Thr Leu Leu Pro Ser Ser Pro
             20                  25                  30

Trp Pro Pro Leu Ala Cys Pro Pro Val Leu Leu His Gln Pro His Cys
         35                  40                  45

Pro Pro Ser Ala Pro Pro Thr Leu Trp Ser Phe
     50                  55



<210> 591
<211> 116
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 591
Val His Ala Glu Ala Gly Arg Leu Cys His Gly Asp Cys Pro Arg Leu
  1               5                  10                  15

Cys Arg Pro Arg Gln Arg Ser Ala Pro Val Gln Val Tyr Thr Xaa Arg
             20                  25                  30

Gln Ala Ala Leu His Gly Arg Pro Gln Arg Asp Pro Cys Val Gly Gly
         35                  40                  45

Pro Arg Pro Leu Arg Cys Ser Arg Asp Cys Gly Gly Gly His Gln Arg
     50                  55                  60

Leu Val Met Pro Gly Thr Trp Thr Gln Ala Trp Gln Arg Arg Gln Val
 65                  70                  75                  80

Val Asn Gly Leu Met Leu Gly Gln Ala Arg Ile His Val Asn Arg Leu
                 85                  90                  95

Glu Gln Ala Val Val Asn Leu Ala Pro Cys Glu Tyr Phe His Thr Cys
            100                 105                 110

Cys Pro Phe Ala
        115
```

<210> 592
<211> 290
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (239)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 592
```
Arg Arg Ser Leu Asn Thr His Gly Ser Gly Val Ser Val Cys Leu Gln
  1               5                  10                  15

Ser Leu Thr Leu Leu Ala Thr Leu Cys Pro Gly Asp Gln Xaa Ser Leu
             20                  25                  30

Gly Leu Leu Thr Pro Cys Tyr Ser Gly Ser Glu Pro Ser Gly Thr Phe
         35                  40                  45

Gly Pro Val Asn Pro Ser Leu Asn Asn Thr Tyr Glu Phe Met Ser Thr
     50                  55                  60

Phe Phe Leu Glu Val Ser Ser Val Phe Pro Asp Phe Tyr Leu His Leu
 65                  70                  75                  80

Gly Gly Asp Glu Val Asp Phe Thr Cys Trp Lys Ser Asn Pro Glu Ile
                 85                  90                  95

Gln Asp Phe Met Arg Lys Lys Gly Phe Gly Glu Asp Phe Lys Gln Leu
            100                 105                 110

Glu Ser Phe Tyr Ile Gln Thr Leu Leu Asp Ile Val Ser Ser Tyr Gly
        115                 120                 125

Lys Gly Tyr Val Val Trp Gln Glu Val Phe Asp Asn Lys Val Lys Ile
    130                 135                 140

Gln Pro Asp Thr Ile Ile Gln Val Trp Arg Glu Asp Ile Pro Val Asn
145                 150                 155                 160

Tyr Met Lys Glu Leu Glu Leu Val Thr Lys Ala Gly Phe Arg Ala Leu
                165                 170                 175

Leu Ser Ala Pro Trp Tyr Leu Asn Arg Ile Ser Tyr Gly Pro Asp Trp
            180                 185                 190
```

Lys Asp Phe Tyr Val Val Glu Pro Leu Ala Phe Glu Gly Thr Pro Glu
195 200 205

Gln Lys Ala Leu Val Ile Gly Gly Glu Ala Cys Met Trp Gly Glu Tyr
210 215 220

Val Asp Asn Thr Asn Leu Val Pro Arg Leu Trp Pro Arg Ala Xaa Ala
225 230 235 240

Val Ala Glu Arg Leu Trp Ser Asn Lys Leu Thr Ser Asp Leu Thr Phe
245 250 255

Ala Tyr Glu Arg Leu Ser His Phe Arg Cys Glu Leu Leu Arg Arg Gly
260 265 270

Val Gln Ala Gln Pro Leu Asn Val Gly Phe Cys Glu Gln Glu Phe Glu
275 280 285

Gln Thr
290

<210> 593
<211> 665
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 593
Asp Ala Asp Gly Arg Met Asp Xaa Leu Val Ser Glu Cys Ser Ala Arg
1 5 10 15

Leu Leu Gln Gln Glu Glu Glu Ile Lys Ser Leu Thr Ala Glu Ile Asp
20 25 30

Arg Leu Lys Asn Cys Gly Cys Leu Gly Ala Ser Pro Asn Leu Glu Gln
35 40 45

Leu Gln Glu Glu Asn Leu Lys Leu Lys Tyr Arg Leu Asn Ile Leu Arg
50 55 60

Lys Ser Leu Gln Ala Glu Arg Asn Lys Pro Thr Lys Asn Met Ile Asn
65 70 75 80

Ile Ile Ser Arg Leu Gln Glu Val Phe Gly His Ala Ile Lys Ala Ala

85 90 95

Tyr Pro Asp Leu Glu Asn Pro Pro Leu Leu Val Thr Pro Ser Gln Gln
100 105 110

Ala Lys Phe Gly Asp Tyr Gln Cys Asn Ser Ala Met Gly Ile Ser Gln
115 120 125

Met Leu Lys Thr Lys Glu Gln Lys Val Asn Pro Arg Glu Ile Ala Glu
130 135 140

Asn Ile Thr Lys His Leu Pro Asp Asn Glu Cys Ile Glu Lys Val Glu
145 150 155 160

Ile Ala Gly Pro Gly Phe Ile Asn Val His Leu Arg Lys Asp Phe Val
165 170 175

Ser Glu Gln Leu Thr Ser Leu Leu Val Asn Gly Val Gln Leu Pro Ala
180 185 190

Leu Gly Glu Asn Lys Lys Val Ile Val Asp Phe Ser Ser Pro Asn Ile
195 200 205

Ala Lys Glu Met His Val Gly His Leu Arg Ser Thr Ile Ile Gly Glu
210 215 220

Ser Ile Ser Arg Leu Phe Glu Phe Ala Gly Tyr Asp Val Leu Arg Leu
225 230 235 240

Asn His Val Gly Asp Trp Gly Thr Gln Phe Gly Met Leu Ile Ala His
245 250 255

Leu Gln Asp Lys Phe Pro Asp Tyr Leu Thr Val Ser Pro Pro Ile Gly
260 265 270

Asp Leu Gln Val Phe Tyr Lys Glu Ser Lys Lys Arg Phe Asp Thr Glu
275 280 285

Glu Glu Phe Lys Lys Arg Ala Tyr Gln Cys Val Val Leu Leu Gln Gly
290 295 300

Lys Asn Pro Asp Ile Thr Lys Ala Trp Lys Leu Ile Cys Asp Val Ser
305 310 315 320

Arg Gln Glu Leu Asn Lys Ile Tyr Asp Ala Leu Asp Val Ser Leu Ile
325 330 335

Glu Arg Gly Glu Ser Phe Tyr Gln Asp Arg Met Asn Asp Ile Val Lys
340 345 350

Glu Phe Glu Asp Arg Gly Phe Val Gln Val Asp Asp Gly Arg Lys Ile

355 360 365

Val Phe Val Pro Gly Cys Ser Ile Pro Leu Thr Ile Val Lys Ser Asp
370 375 380

Gly Gly Tyr Thr Tyr Asp Thr Ser Asp Leu Ala Ala Ile Lys Gln Arg
385 390 395 400

Leu Phe Glu Glu Lys Ala Asp Met Ile Ile Tyr Val Val Asp Asn Gly
405 410 415

Gln Ser Val His Phe Gln Thr Ile Phe Ala Ala Ala Gln Met Ile Gly
420 425 430

Trp Tyr Asp Pro Lys Val Thr Arg Val Phe His Ala Gly Phe Gly Val
435 440 445

Val Leu Gly Glu Asp Lys Lys Lys Phe Lys Thr Arg Ser Gly Glu Thr
450 455 460

Val Arg Leu Met Asp Leu Leu Gly Glu Gly Leu Lys Arg Ser Met Asp
465 470 475 480

Lys Leu Lys Glu Lys Glu Arg Asp Lys Val Leu Thr Ala Glu Glu Leu
485 490 495

Asn Ala Ala Gln Thr Ser Val Ala Tyr Gly Cys Ile Lys Tyr Ala Asp
500 505 510

Leu Ser His Asn Arg Leu Asn Asp Tyr Ile Phe Ser Phe Asp Lys Met
515 520 525

Leu Asp Asp Arg Gly Asn Thr Ala Ala Tyr Leu Leu Tyr Ala Phe Thr
530 535 540

Arg Ile Arg Ser Ile Ala Arg Leu Ala Asn Ile Asp Glu Glu Met Leu
545 550 555 560

Gln Lys Ala Ala Arg Glu Thr Lys Ile Leu Leu Asp His Glu Lys Glu
565 570 575

Trp Lys Leu Gly Arg Cys Ile Leu Arg Phe Pro Glu Ile Leu Gln Lys
580 585 590

Ile Leu Asp Asp Leu Phe Leu His Thr Leu Cys Asp Tyr Ile Tyr Glu
595 600 605

Leu Ala Thr Ala Phe Thr Glu Phe Tyr Asp Ser Cys Tyr Cys Val Glu
610 615 620

Lys Asp Arg Gln Thr Gly Lys Ile Leu Lys Val Asn Met Trp Arg Met

625 630 635 640

Leu Leu Cys Glu Ala Val Ala Ala Val Met Ala Lys Gly Phe Asp Ile
645 650 655

Leu Gly Ile Lys Pro Val Gln Arg Met
660 665

<210> 594
<211> 116
<212> PRT
<213> Homo sapiens

<400> 594
Thr Val Thr Glu Thr Thr Val Thr Val Thr Thr Glu Pro Glu Asn Arg
1 5 10 15

Ser Leu Thr Ile Lys Leu Arg Lys Arg Lys Pro Glu Lys Lys Val Glu
20 25 30

Trp Thr Ser Asp Thr Val Asp Asn Glu His Met Gly Arg Arg Ser Ser
35 40 45

Lys Cys Cys Cys Ile Tyr Glu Lys Pro Arg Ala Phe Gly Glu Ser Ser
50 55 60

Thr Glu Ser Asp Glu Glu Glu Glu Glu Gly Cys Gly His Thr His Cys
65 70 75 80

Val Arg Gly His Arg Lys Gly Arg Arg Arg Ala Thr Leu Gly Pro Thr
85 90 95

Pro Thr Thr Pro Pro Gln Pro Pro Asp Pro Ser Gln Pro Pro Pro Gly
100 105 110

Pro Met Gln His
115

<210> 595
<211> 294
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (269)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (278)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 595
Thr Gln Leu Arg Val Ser Glu Arg Glu Gly Pro Gly Asp Pro Gln Arg
1 5 10 15

Phe Ser Asp His Thr Leu Arg Thr Pro Arg Leu Glu Asp Arg Pro Gly
20 25 30

Asp Ala Met Trp Gly Glu Gly Leu Arg Ala Trp Cys Arg Phe Val Glu
35 40 45

Asn Arg Trp Cys Leu Lys Arg Val Ser Ala Pro Leu His Leu Gly Leu
50 55 60

Leu Gly Cys Pro Asp Ala Glu Ala His Phe Pro Ala Met Leu Thr Leu
65 70 75 80

Pro Leu Ser Pro Pro Ser Arg Lys Met Ala Thr Asn Phe Leu Ala His
85 90 95

Glu Lys Ile Trp Phe Asp Lys Phe Lys Tyr Asp Asp Ala Glu Arg Arg
100 105 110

Phe Tyr Glu Gln Met Asn Gly Pro Val Ala Gly Ala Ser Arg Gln Glu
115 120 125

Asn Gly Ala Ser Val Ile Leu Arg Asp Ile Ala Arg Ala Arg Glu Asn
130 135 140

Ile Gln Lys Ser Leu Ala Gly Ser Ser Gly Pro Gly Ala Ser Ser Gly
145 150 155 160

Thr Ser Gly Asp His Gly Glu Leu Val Val Arg Ile Ala Ser Leu Glu
165 170 175

Val Glu Asn Gln Ser Leu Arg Gly Val Val Gln Glu Leu Gln Gln Ala
180 185 190

Ile Ser Lys Leu Glu Ala Arg Leu Asn Val Leu Glu Lys Ser Ser Pro
195 200 205

Gly His Arg Ala Thr Ala Pro Gln Thr Gln His Val Ser Pro Met Arg
210 215 220

Gln Val Glu Pro Pro Ala Lys Lys Pro Ala Thr Pro Ala Glu Asp Asp
225 230 235 240

```
Glu Asp Asp Asp Ile Asp Leu Phe Gly Ser Asp Asn Glu Glu Glu Asp
                245                 250                 255

Lys Glu Ala Ala Gln Leu Arg Glu Glu Arg Leu Arg Xaa Tyr Ala Glu
            260                 265                 270

Lys Lys Ala Lys Lys Xaa Ala Leu Val Ala Lys Ser Ser Ile Leu Leu
        275                 280                 285

Asp Phe Lys Pro Trp Gly
    290
```

<210> 596
<211> 134
<212> PRT
<213> Homo sapiens

<400> 596

```
Val Ser Arg Leu Gly Leu Leu Thr Pro Leu Gly Cys Ser Phe Gly Thr
  1               5                  10                  15

Asp Glu Trp Leu Cys Pro Val Thr Ala Leu Ser Leu Pro Gly Gly Tyr
             20                  25                  30

Val His Ser Arg Pro Leu Pro Arg Leu Arg Pro Met Arg Tyr Gly Asp
         35                  40                  45

Thr Leu Ala Pro Arg Ser Trp Arg His Arg Pro Leu Pro Trp His Ser
     50                  55                  60

Ser Phe Ala Gly Asp Pro Pro Leu Pro Lys Ala Leu Ser Pro Cys Ser
 65                  70                  75                  80

His Ser Arg Arg Thr Ala Ala Arg Ala Ser Gly Ser Leu Ala Thr Gly
                 85                  90                  95

Phe Glu Arg Leu His Ser Trp Gly Leu Glu Gly Gly Val Pro Lys Ala
            100                 105                 110

Leu Ser Lys Ser Gln Ser Ser Ser His Gln Ser Leu Tyr Lys Val Leu
        115                 120                 125

Gly Pro Glu Ala Leu Pro
    130
```

<210> 597

<211> 91
<212> PRT
<213> Homo sapiens

<400> 597
Glu Gly Pro Glu Gly Ala Asn Leu Phe Ile Tyr His Leu Pro Gln Glu
1   5   10   15

Phe Gly Asp Gln Asp Ile Leu Gln Met Phe Met Pro Phe Gly Asn Val
            20   25   30

Ile Ser Ala Lys Val Phe Ile Asp Lys Gln Thr Asn Leu Ser Lys Cys
        35   40   45

Phe Gly Phe Val Ser Tyr Asp Asn Pro Val Ser Ala Gln Ala Ala Ile
    50   55   60

Gln Ala Met Asn Gly Phe Gln Ile Gly Met Lys Arg Leu Lys Val Gln
65   70   75   80

Leu Lys Arg Ser Lys Asn Asp Ser Lys Pro Tyr
                85   90

<210> 598
<211> 68
<212> PRT
<213> Homo sapiens

<400> 598
Arg Pro Thr Arg Pro Glu Lys Val Gly Ser Gly Gly Ser Ser Val Gly
1   5   10   15

Ser Gly Asp Ala Ser Ser Ser Arg His His His Arg Arg Arg Arg Phe
            20   25   30

His Leu Pro Gln Gln Pro Leu Leu Gln Arg Glu Val Trp Cys Val Gly
        35   40   45

Thr Thr Gly Asn Ala Asn Gln Ala Gln Ser Ser Thr Glu Gln Thr Leu
    50   55   60

Leu Lys Pro Lys
65

<210> 599
<211> 119
<212> PRT

<213> Homo sapiens

<220>
<221> SITE
<222> (58)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (88)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (98)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (99)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 599
```
Phe Gly Arg Asp Gln Val Tyr Leu Ser Tyr Asn Asn Val Ser Ser Leu
  1               5                  10                  15

Lys Met Leu Val Ala Lys Asp Asn Trp Val Leu Ser Ser Glu Ile Ser
             20                  25                  30

Gln Val Arg Leu Tyr Thr Leu Glu Asp Asp Lys Phe Leu Ser Phe His
         35                  40                  45

Met Glu Met Val Val His Val Asp Ala Xaa Gln Ala Phe Leu Leu Leu
     50                  55                  60

Ser Asp Leu Xaa Gln Arg Pro Glu Trp Asp Lys His Tyr Arg Ser Val
 65                  70                  75                  80

Glu Leu Val Gln Gln Val Asp Xaa Gly Arg Arg His Leu Pro Arg His
                 85                  90                  95

Gln Xaa Xaa Pro Arg Arg Ser His Lys Ala Pro Gly Leu Arg Asp Pro
            100                 105                 110

Gly Leu Glu Ala Glu Ala Leu
        115
```

<210> 600
<211> 177
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (69)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 600
Xaa Glu Arg Leu Arg Ala Gln Xaa Glu Lys Ser Arg Asp Ser Gln Pro
1   5   10   15

Arg Leu Pro Leu Arg Phe Pro Ser Trp Arg Gly Pro Trp Cys Gly Ile
            20   25   30

Glu Ile Ala Gly Tyr Gly Ala Glu Val Phe Arg Gln Tyr Trp Asp Ile
        35   40   45

Pro Asp Gly Thr Asp Cys His Arg Lys Ala Tyr Ser Thr Thr Ser Ile
    50   55   60

Ala Ser Val Ala Xaa Leu Thr Ala Ala Ala Tyr Arg Val Thr Leu Asn
65   70   75   80

Pro Pro Gly Thr Phe Leu Glu Gly Val Ala Lys Val Gly Gln Tyr Thr
                85   90   95

Phe Thr Ala Ala Ala Val Gly Ala Val Phe Gly Leu Thr Thr Cys Ile
            100   105   110

Ser Ala His Val Arg Glu Lys Pro Asp Asp Pro Leu Asn Tyr Phe Leu

115 120 125

Gly Gly Cys Ala Gly Gly Xaa Thr Leu Gly Ala Arg Thr His Asn Tyr
130 135 140

Gly Ile Gly Ala Ala Ala Cys Val Tyr Phe Gly Ile Ala Ala Ser Leu
145 150 155 160

Val Lys Met Gly Arg Leu Glu Gly Trp Glu Val Phe Ala Lys Pro Lys
165 170 175

Val

<210> 601
<211> 218
<212> PRT
<213> Homo sapiens

<400> 601
Arg Gly Gly Gly Gly Gly Ala Ser Ser Cys Cys Cys Cys Ala Pro Ser
1 5 10 15

Pro Arg Gly Arg Pro Val Pro Ala Arg Thr Pro Arg Arg Cys Pro Arg
20 25 30

Pro Ser Pro Gly Pro Ala Met Gly Leu Thr Val Ser Ala Leu Phe Ser
35 40 45

Arg Ile Phe Gly Lys Lys Gln Met Arg Ile Leu Met Val Gly Leu Asp
50 55 60

Ala Ala Gly Lys Thr Thr Ile Leu Tyr Lys Leu Lys Leu Gly Glu Ile
65 70 75 80

Val Thr Thr Ile Pro Thr Ile Gly Phe Asn Val Glu Thr Val Glu Tyr
85 90 95

Lys Asn Ile Cys Phe Thr Val Trp Asp Val Gly Gly Gln Asp Lys Ile
100 105 110

Arg Pro Leu Trp Arg His Tyr Phe Gln Asn Thr Gln Gly Leu Ile Phe
115 120 125

Val Val Asp Ser Asn Asp Arg Glu Arg Val Gln Glu Ser Ala Asp Glu
130 135 140

Leu Gln Lys Met Leu Gln Glu Asp Glu Leu Arg Asp Ala Val Leu Leu
145 150 155 160

Val Phe Ala Asn Lys Gln Asp Met Pro Asn Ala Met Pro Val Ser Glu
165 170 175

Leu Thr Asp Lys Leu Gly Leu Gln His Leu Arg Ser Arg Thr Trp Tyr
180 185 190

Val Gln Ala Thr Cys Ala Thr Gln Gly Thr Gly Leu Tyr Asp Gly Leu
195 200 205

Asp Trp Leu Ser His Glu Leu Ser Lys Arg
210 215

<210> 602
<211> 829
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (32)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (454)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 602
Pro Gly Gln Ala Gly Ala Glu Gly His Val Arg Cys Cys Pro Gly Glu
1 5 10 15

Glu Gln Lys Ala Gly Gly Glu Arg Arg Cys Pro Gly Pro Gln Arg Xaa
20 25 30

Gly Ala Ala Leu Gly Pro Gly Pro Gly Glu Ala Arg Leu Asp Tyr Ser
35 40 45

Glu Phe Phe Thr Glu Asp Val Gly Gln Leu Pro Gly Leu Thr Ile Trp
50 55 60

Gln Ile Glu Asn Phe Val Pro Val Leu Val Glu Glu Ala Phe His Gly
65 70 75 80

Lys Phe Tyr Glu Ala Asp Cys Tyr Ile Val Leu Lys Thr Phe Leu Asp
85 90 95

Asp Ser Gly Ser Leu Asn Trp Glu Ile Tyr Tyr Trp Ile Gly Gly Glu
100 105 110

Ala Thr Leu Asp Lys Lys Ala Cys Ser Ala Ile His Ala Val Asn Leu
115 120 125

Arg Asn Tyr Leu Gly Ala Glu Cys Arg Thr Val Arg Glu Glu Met Gly
130 135 140

Asp Glu Ser Glu Glu Phe Leu Gln Val Phe Asp Asn Asp Ile Ser Tyr
145 150 155 160

Ile Glu Gly Gly Thr Ala Ser Gly Phe Tyr Thr Val Glu Asp Thr His
165 170 175

Tyr Val Thr Arg Met Tyr Arg Val Tyr Gly Lys Lys Asn Ile Lys Leu
180 185 190

Glu Pro Val Pro Leu Lys Gly Thr Ser Leu Asp Pro Arg Phe Val Phe
195 200 205

Leu Leu Asp Arg Gly Leu Asp Ile Tyr Val Trp Arg Gly Ala Gln Ala
210 215 220

Thr Leu Ser Ser Thr Thr Lys Ala Arg Leu Phe Ala Glu Lys Ile Asn
225 230 235 240

Lys Asn Glu Arg Lys Gly Lys Ala Glu Ile Thr Leu Leu Val Gln Gly
245 250 255

Gln Glu Leu Pro Glu Phe Trp Glu Ala Leu Gly Gly Glu Pro Ser Glu
260 265 270

Ile Lys Lys His Val Pro Glu Asp Phe Trp Pro Pro Gln Pro Lys Leu
275 280 285

Tyr Lys Val Gly Leu Gly Leu Gly Tyr Leu Glu Leu Pro Gln Ile Asn
290 295 300

Tyr Lys Leu Ser Val Glu His Lys Gln Arg Pro Lys Val Glu Leu Met
305 310 315 320

Pro Arg Met Arg Leu Leu Gln Ser Leu Leu Asp Thr Arg Cys Val Asn
325 330 335

Ile Leu Asp Cys Trp Ser Asp Val Phe Ile Trp Leu Gly Arg Lys Ser
340 345 350

Pro Arg Leu Val Arg Ala Ala Ala Leu Lys Leu Gly Gln Glu Leu Cys
355 360 365

Gly Met Leu His Arg Pro Arg His Ala Thr Val Ser Arg Ser Leu Glu
370 375 380

Gly Thr Glu Ala Gln Val Phe Lys Ala Lys Phe Lys Asn Trp Asp Asp
385 390 395 400

Val Leu Thr Val Asp Tyr Thr Arg Asn Ala Glu Ala Val Leu Gln Ser
405 410 415

Pro Gly Leu Ser Gly Lys Val Lys Arg Asp Ala Glu Lys Lys Asp Gln
420 425 430

Met Lys Ala Asp Leu Thr Ala Leu Phe Leu Pro Arg Gln Pro Pro Met
435 440 445

Ser Leu Ala Glu Ala Xaa Gln Leu Met Glu Glu Trp Asn Glu Asp Leu
450 455 460

Asp Gly Met Glu Gly Phe Val Leu Glu Gly Lys Lys Phe Ala Arg Leu
465 470 475 480

Pro Glu Glu Glu Phe Gly His Phe Tyr Thr Gln Asp Cys Tyr Val Phe
485 490 495

Leu Cys Arg Tyr Trp Val Pro Val Glu Tyr Glu Glu Glu Glu Lys Lys
500 505 510

Glu Asp Lys Glu Glu Lys Ala Glu Gly Lys Glu Gly Glu Glu Ala Thr
515 520 525

Ala Glu Ala Glu Glu Lys Gln Pro Glu Glu Asp Phe Gln Cys Ile Val
530 535 540

Tyr Phe Trp Gln Gly Arg Glu Ala Ser Asn Met Gly Trp Leu Thr Phe
545 550 555 560

Thr Phe Ser Leu Gln Lys Lys Phe Glu Ser Leu Phe Pro Gly Lys Leu
565 570 575

Glu Val Val Arg Met Thr Gln Gln Gln Glu Asn Pro Lys Phe Leu Ser
580 585 590

His Phe Lys Arg Lys Phe Ile Ile His Arg Gly Lys Arg Lys Ala Val
595 600 605

Gln Gly Ala Gln Gln Pro Ser Leu Tyr Gln Ile Arg Thr Asn Gly Ser
610 615 620

Ala Leu Cys Thr Arg Cys Ile Gln Ile Asn Thr Asp Ser Ser Leu Leu
625 630 635 640

Asn Ser Glu Phe Cys Phe Ile Leu Lys Val Pro Phe Glu Ser Glu Asp
645 650 655

Asn Gln Gly Ile Val Tyr Ala Trp Val Gly Arg Ala Ser Asp Pro Asp
660 665 670

Glu Ala Lys Leu Ala Glu Asp Ile Leu Asn Thr Met Phe Asp Thr Ser
675 680 685

Tyr Ser Lys Gln Val Ile Asn Glu Gly Glu Glu Pro Glu Asn Phe Phe
690 695 700

Trp Val Gly Ile Gly Ala Gln Lys Pro Tyr Asp Asp Asp Ala Glu Tyr
705 710 715 720

Met Lys His Thr Arg Leu Phe Arg Cys Ser Asn Glu Lys Gly Tyr Phe
725 730 735

Ala Val Thr Glu Lys Cys Ser Asp Phe Cys Gln Asp Asp Leu Ala Asp
740 745 750

Asp Asp Ile Met Leu Leu Asp Asn Gly Gln Glu Val Tyr Met Trp Val
755 760 765

Gly Thr Gln Thr Ser Gln Val Glu Ile Lys Leu Ser Leu Lys Ala Cys
770 775 780

Gln Val Tyr Ile Gln His Met Arg Ser Lys Glu His Glu Arg Pro Arg
785 790 795 800

Arg Leu Arg Leu Val Arg Lys Gly Asn Glu Gln His Ala Phe Thr Arg
805 810 815

Cys Phe His Ala Trp Ser Ala Phe Cys Lys Ala Leu Ala
820 825

<210> 603
<211> 221
<212> PRT
<213> Homo sapiens

<400> 603
Thr Glu Pro Pro Leu Ser Cys Cys Leu Pro Ala Thr Tyr Pro Ala Asp
1 5 10 15

Met Gly Thr Ala Gly Ala Met Gln Leu Cys Trp Val Ile Leu Gly Phe
20 25 30

Leu Leu Phe Arg Gly His Asn Ser Gln Pro Thr Met Thr Gln Thr Ser
35 40 45

Ser Ser Gln Gly Gly Leu Gly Gly Leu Ser Leu Thr Thr Glu Pro Val
50 55 60

Ser Ser Asn Pro Gly Tyr Ile Pro Ser Ser Glu Ala Asn Arg Pro Ser
65 70 75 80

His Leu Ser Ser Thr Gly Thr Pro Gly Ala Gly Val Pro Ser Ser Gly
85 90 95

Arg Asp Gly Gly Thr Ser Arg Asp Thr Phe Gln Thr Val Pro Pro Asn
100 105 110

Ser Thr Thr Met Ser Leu Ser Met Arg Glu Asp Ala Thr Ile Leu Pro
115 120 125

Ser Pro Thr Ser Glu Thr Val Leu Thr Val Ala Ala Phe Gly Val Ile
130 135 140

Ser Phe Ile Val Ile Leu Val Val Val Val Ile Ile Leu Val Gly Val
145 150 155 160

Val Ser Leu Arg Phe Lys Cys Arg Lys Ser Lys Glu Ser Glu Asp Pro
165 170 175

Gln Lys Pro Gly Ser Ser Gly Leu Ser Glu Ser Cys Ser Thr Ala Asn
180 185 190

Gly Glu Lys Asp Ser Ile Thr Leu Ile Ser Met Lys Asn Ile Asn Met
195 200 205

Asn Asn Gly Lys Gln Ser Leu Ser Ala Glu Lys Val Leu
210 215 220

<210> 604
<211> 97
<212> PRT
<213> Homo sapiens

<400> 604
Ser Cys Gly Leu Ser Leu Ile Lys Met Thr Thr Ser Gln Lys His Arg
1 5 10 15

Asp Phe Val Ala Glu Pro Met Gly Glu Lys Pro Val Gly Ser Leu Ala
20 25 30

Gly Ile Gly Glu Val Leu Gly Lys Lys Leu Glu Glu Arg Gly Phe Asp
35 40 45

Lys Ala Tyr Val Val Leu Gly Gln Phe Leu Val Leu Lys Lys Asp Glu

```
    50                  55                  60

Asp Leu Phe Arg Glu Trp Leu Lys Asp Thr Cys Gly Ala Asn Ala Lys
 65                  70                  75                  80

Gln Ser Arg Asp Cys Phe Gly Cys Leu Arg Glu Trp Cys Asp Ala Phe
                85                  90                  95

Leu



<210> 605
<211> 266
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 605
Gly Pro Arg Arg Leu Gly Ala Leu His Ala Ala Ala Thr Gly Ala Arg
  1               5                  10                  15

Cys Leu Val Glu Leu Leu Val Ala His Gly Ala Asp Leu Asn Ala Lys
             20                  25                  30

Ser Leu Met Asp Glu Thr Pro Leu Asp Val Cys Gly Asp Glu Glu Val
         35                  40                  45

Arg Ala Lys Leu Leu Glu Leu Lys His Lys His Asp Ala Leu Leu Arg
    50                  55                  60

Ala Gln Ser Arg Gln Arg Ser Leu Leu Arg Arg Arg Thr Ser Ser Ala
 65                  70                  75                  80

Gly Ser Arg Xaa Lys Val Val Arg Arg Val Ser Leu Thr Gln Arg Thr
                85                  90                  95

Asp Leu Tyr Arg Lys Gln His Ala Gln Glu Ala Ile Val Trp Gln Gln
            100                 105                 110

Pro Pro Pro Thr Ser Pro Glu Pro Pro Glu Asp Asn Asp Asp Arg Gln
        115                 120                 125

Thr Gly Ala Glu Leu Arg Pro Pro Pro Pro Glu Glu Asp Asn Pro Glu
    130                 135                 140
```

Val Val Arg Pro His Asn Gly Arg Val Gly Gly Ser Pro Val Arg His
145 150 155 160

Leu Tyr Ser Lys Arg Leu Asp Arg Ser Val Ser Tyr Gln Leu Ser Pro
165 170 175

Leu Asp Ser Thr Thr Pro His Thr Leu Val His Asp Lys Ala His His
180 185 190

Thr Leu Ala Asp Leu Lys Arg Gln Arg Ala Ala Ala Lys Leu Gln Arg
195 200 205

Pro Pro Pro Glu Gly Pro Glu Ser Pro Glu Thr Ala Glu Pro Gly Leu
210 215 220

Pro Gly Asp Thr Val Thr Pro Gln Pro Asp Cys Gly Phe Arg Ala Gly
225 230 235 240

Gly Asp Pro Pro Leu Leu Lys Leu Thr Ala Pro Ala Val Glu Ala Pro
245 250 255

Val Glu Arg Arg Pro Cys Cys Leu Leu Met
260 265

<210> 606
<211> 331
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (91)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (285)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 606
His Asp Ser Cys Phe Val Glu Met Gln Ala Gln Lys Val Met His Val
1 5 10 15

Ser Ser Ala Glu Leu Asn Tyr Ser Leu Pro Tyr Asp Ser Lys His Gln
20 25 30

Ile Arg Asn Ala Ser Asn Val Lys His His Asp Ser Ser Ala Leu Gly
35 40 45

```
Val Tyr Ser Tyr Ile Pro Leu Val Glu Asn Pro Tyr Phe Ser Ser Trp
    50                  55                  60

Pro Pro Ser Gly Thr Ser Ser Lys Met Ser Leu Asp Leu Pro Glu Lys
65                  70                  75                  80

Gln Asp Gly Thr Val Phe Pro Ser Ser Leu Xaa Pro Thr Ser Ser Thr
                85                  90                  95

Ser Leu Phe Ser Tyr Tyr Asn Ser His Asp Ser Leu Ser Leu Asn Ser
            100                 105                 110

Pro Thr Asn Ile Ser Ser Leu Leu Asn Gln Glu Ser Ala Val Leu Ala
        115                 120                 125

Thr Ala Pro Arg Ile Asp Asp Glu Ile Pro Pro Pro Leu Pro Val Arg
    130                 135                 140

Thr Pro Glu Ser Phe Ile Val Val Glu Glu Ala Gly Glu Phe Ser Pro
145                 150                 155                 160

Asn Val Pro Lys Ser Leu Ser Ser Ala Val Lys Val Lys Ile Gly Thr
                165                 170                 175

Ser Leu Glu Trp Gly Gly Thr Ser Glu Pro Lys Lys Phe Asp Asp Ser
            180                 185                 190

Val Ile Leu Arg Pro Ser Lys Ser Val Lys Leu Arg Ser Pro Lys Ser
        195                 200                 205

Glu Leu His Gln Asp Arg Ser Ser Pro Pro Pro Pro Leu Pro Glu Arg
    210                 215                 220

Thr Leu Glu Ser Phe Phe Leu Ala Asp Glu Asp Cys Met Gln Ala Gln
225                 230                 235                 240

Ser Ile Glu Thr Tyr Ser Thr Ser Tyr Pro Asp Thr Met Glu Asn Ser
                245                 250                 255

Thr Ser Ser Lys Gln Thr Leu Lys Thr Pro Gly Lys Ser Phe Thr Arg
            260                 265                 270

Ser Lys Ser Leu Lys Ile Leu Arg Asn Met Lys Lys Xaa Ile Cys Asn
        275                 280                 285

Ser Cys Pro Pro Asn Lys Pro Ala Glu Ser Val Gln Ser Asn Asn Ser
    290                 295                 300

Ser Ser Phe Leu Asn Phe Gly Phe Ala Asn Arg Phe Ser Lys Pro Lys
305                 310                 315                 320
```

```
Gly Pro Arg Asn Pro Pro Pro Thr Trp Asn Ile
                325                 330



<210> 607
<211> 192
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 607
Ala Ala Pro Ser Glu Pro Lys Ala Arg Gly Gly His Gly Gly Ala Leu
  1               5                  10                  15

Ala Arg Leu Glu Thr Met Pro Lys Leu Gln Gly Phe Glu Phe Trp Ser
             20                  25                  30

Arg Thr Leu Arg Gly Ala Arg His Val Val Ala Pro Met Val Asp Gln
         35                  40                  45

Ser Glu Leu Ala Trp Arg Leu Leu Ser Arg Arg His Gly Ala Gln Leu
     50                  55                  60

Cys Tyr Thr Pro Met Leu His Ala Gln Val Phe Val Arg Xaa Ala Asn
 65                  70                  75                  80

Tyr Arg Lys Glu Asn Leu Tyr Cys Glu Val Cys Pro Glu Asp Arg Pro
                 85                  90                  95

Leu Ile Val Gln Phe Cys Ala Asn Asp Pro Glu Val Phe Val Gln Ala
            100                 105                 110

Ala Leu Leu Ala Gln Asp Tyr Cys Asp Ala Ile Asp Leu Asn Leu Gly
        115                 120                 125

Cys Pro Gln Met Ile Ala Lys Arg Gly His Tyr Gly Ala Phe Leu Gln
    130                 135                 140

Asp Glu Trp Asp Leu Leu Gln Arg Met Ile Leu Leu Ala His Glu Lys
145                 150                 155                 160

Leu Ser Val Pro Val Thr Cys Lys Ile Arg Val Phe Pro Glu Ile Asp
                165                 170                 175

Lys Thr Val Ser Thr Pro Arg Cys Trp Arg Arg Pro Ala Ala Ser Cys
            180                 185                 190
```

<210> 608
<211> 415
<212> PRT
<213> Homo sapiens

<400> 608
His Ile Lys Cys Pro His Ser Lys Tyr Gly Cys Thr Phe Ile Gly Asn
1 5 10 15

Gln Asp Thr Tyr Glu Thr His Leu Glu Thr Cys Arg Phe Glu Gly Leu
20 25 30

Lys Glu Phe Leu Gln Gln Thr Asp Asp Arg Phe His Glu Met His Val
35 40 45

Ala Leu Ala Gln Lys Asp Gln Glu Ile Ala Phe Leu Arg Ser Met Leu
50 55 60

Gly Lys Leu Ser Glu Lys Ile Asp Gln Leu Glu Lys Ser Leu Glu Leu
65 70 75 80

Lys Phe Asp Val Leu Asp Glu Asn Gln Ser Lys Leu Ser Glu Asp Leu
85 90 95

Met Glu Phe Arg Arg Asp Ala Ser Met Leu Asn Asp Glu Leu Ser His
100 105 110

Ile Asn Ala Arg Leu Asn Met Gly Ile Leu Gly Ser Tyr Asp Pro Gln
115 120 125

Gln Ile Phe Lys Cys Lys Gly Thr Phe Val Gly His Gln Gly Pro Val
130 135 140

Trp Cys Leu Cys Val Tyr Ser Met Gly Asp Leu Leu Phe Ser Gly Ser
145 150 155 160

Ser Asp Lys Thr Ile Lys Val Trp Asp Thr Cys Thr Thr Tyr Lys Cys
165 170 175

Gln Lys Thr Leu Glu Gly His Asp Gly Ile Val Leu Ala Leu Cys Ile
180 185 190

Gln Gly Cys Lys Leu Tyr Ser Gly Ser Ala Asp Cys Thr Ile Ile Val
195 200 205

```
Trp Asp Ile Gln Asn Leu Gln Lys Val Asn Thr Ile Arg Ala His Asp
    210                 215                 220

Asn Pro Val Cys Thr Leu Val Ser Ser His Asn Val Leu Phe Ser Gly
225                 230                 235                 240

Ser Leu Lys Ala Ile Lys Val Trp Asp Ile Val Gly Thr Glu Leu Lys
                245                 250                 255

Leu Lys Lys Glu Leu Thr Gly Leu Asn His Trp Val Arg Ala Leu Val
            260                 265                 270

Ala Ala Gln Ser Tyr Leu Tyr Ser Gly Ser Tyr Gln Thr Ile Lys Ile
        275                 280                 285

Trp Asp Ile Arg Thr Leu Asp Cys Ile His Val Leu Gln Thr Ser Gly
    290                 295                 300

Gly Ser Val Tyr Ser Ile Ala Val Thr Asn His His Ile Val Cys Gly
305                 310                 315                 320

Thr Tyr Glu Asn Leu Ile His Val Trp Asp Ile Glu Ser Lys Glu Gln
                325                 330                 335

Val Arg Thr Leu Thr Gly His Val Gly Thr Val Tyr Ala Leu Ala Val
            340                 345                 350

Ile Ser Thr Pro Asp Gln Thr Lys Val Phe Ser Ala Ser Tyr Asp Arg
        355                 360                 365

Ser Leu Arg Val Trp Ser Met Asp Asn Met Ile Cys Thr Gln Thr Leu
    370                 375                 380

Leu Arg His Gln Gly Ser Val Thr Ala Leu Ala Val Ser Arg Gly Arg
385                 390                 395                 400

Leu Phe Ser Gly Ala Val Asp Ser Thr Val Lys Val Trp Thr Cys
                405                 410                 415
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<210> 609
<211> 48
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (27)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (34)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 609
Phe Ser Glu Leu Asn Gln Cys Phe Tyr Ile Cys Phe Phe Phe Tyr Ala
1 5 10 15

Ser Trp Lys Trp Arg Met Lys Ile Gln Leu Xaa Cys Ser Asn Ser Arg
20 25 30

Arg Xaa Val Ser Thr Glu Lys Gly Thr Cys Phe Phe Thr Pro Glu Leu
35 40 45

<210> 610
<211> 241
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (13)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (37)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 610

```
Xaa Asp Xaa Gly Arg Pro Xaa Arg Thr Ala Glu Ser Xaa Phe Gly Ile
1               5                   10                  15

Asn Leu Lys Gly Pro Lys Ile Lys Gly Gly Ala Asp Val Ser Gly Gly
            20                  25                  30

Val Ser Ala Pro Xaa Ile Ser Leu Gly Glu Gly His Leu Ser Val Lys
        35                  40                  45

Gly Ser Gly Gly Glu Trp Lys Gly Pro Gln Val Ser Ser Ala Leu Asn
    50                  55                  60

Leu Asp Thr Ser Lys Phe Ala Gly Gly Leu His Phe Ser Gly Pro Lys
65                  70                  75                  80

Val Glu Gly Gly Val Lys Gly Gly Gln Ile Gly Leu Gln Ala Pro Gly
                85                  90                  95

Leu Ser Val Ser Gly Pro Gln Gly His Leu Glu Ser Gly Ser Gly Lys
            100                 105                 110

Val Thr Phe Pro Lys Met Lys Ile Pro Lys Phe Thr Phe Ser Gly Arg
        115                 120                 125

Glu Leu Val Gly Arg Glu Met Gly Val Asp Val His Phe Pro Lys Ala
    130                 135                 140

Glu Ala Ser Ile Gln Ala Gly Ala Gly Asp Gly Glu Trp Glu Glu Ser
145                 150                 155                 160

Glu Val Lys Leu Lys Lys Ser Lys Ile Lys Met Pro Lys Phe Asn Phe
                165                 170                 175

Ser Lys Pro Lys Gly Lys Gly Gly Val Thr Gly Ser Pro Glu Ala Ser
            180                 185                 190

Ile Ser Gly Ser Lys Gly Asp Leu Lys Ser Ser Lys Ala Ser Leu Gly
        195                 200                 205

Ser Leu Glu Gly Glu Ala Glu Ala Glu Ala Ser Ser Pro Lys Gly Lys
    210                 215                 220

Phe Ser Leu Phe Lys Ser Lys Lys Pro Arg His Arg Cys Lys Phe Ile
225                 230                 235                 240

Gln
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<210> 611

<211> 77
<212> PRT
<213> Homo sapiens

<400> 611
His Tyr Arg Arg Tyr Ala Cys Arg Tyr Arg Ser Gly Ile Pro Gly Ser
1 5 10 15

Thr His Ala Ser Gly Val Ala Asp Gly Gly Gln Val Phe Leu Phe Pro
20 25 30

Glu Thr Gly Ser Val Gln Thr Ala Asn Ala His Arg Trp Pro Arg Gly
35 40 45

Gly Gly Ser Gln Gly Val Trp Val Phe Leu Gly Phe Phe Ser Val Val
50 55 60

Ser Phe Thr Gln Gly Trp Trp Ser Gln Pro Val Trp Cys
65 70 75

<210> 612
<211> 137
<212> PRT
<213> Homo sapiens

<400> 612
Leu Gln Val Pro Val Arg Asn Ser Gly Ser Pro Thr Arg Gln Ala Ala
1 5 10 15

Ala Met Thr Phe Cys Arg Leu Leu Asn Arg Cys Gly Glu Ala Ala Arg
20 25 30

Ser Leu Pro Leu Gly Ala Arg Cys Phe Gly Val Arg Val Ser Pro Thr
35 40 45

Gly Glu Lys Val Thr His Thr Gly Gln Val Tyr Asp Asp Lys Asp Tyr
50 55 60

Arg Arg Ile Arg Phe Val Gly Arg Gln Lys Glu Val Asn Glu Asn Phe
65 70 75 80

Ala Ile Asp Leu Ile Ala Glu Gln Pro Val Ser Glu Val Glu Thr Arg
85 90 95

Val Ile Ala Cys Asp Gly Gly Gly Gly Ala Leu Gly His Pro Lys Val
100 105 110

Tyr Ile Asn Leu Asp Lys Glu Thr Lys Thr Gly Thr Cys Gly Tyr Cys
115 120 125

Gly Leu Gln Phe Arg Gln His His His
    130   135

<210> 613
<211> 122
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (50)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (75)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (80)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (85)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (98)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (111)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (116)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 613
Tyr Ser Thr Asp Asn Asn Asn Asn Trp Tyr Ser Ile Phe Tyr Leu His
1 5 10 15

Ser Ser Phe Leu Gly Glu Asn Ala Glu Lys Leu Leu Gln Phe Lys Arg
20 25 30

Trp Phe Trp Ser Ile Val Glu Lys Met Ser Met Thr Glu Arg Gln Asp
35 40 45

Leu Xaa Tyr Phe Trp Thr Ser Ser Pro Ser Leu Pro Ala Ser Glu Glu
50 55 60

Gly Phe Gln Pro Met Pro Ser Ile Thr Ile Xaa Pro Pro Asp Asp Xaa
65 70 75 80

His Leu Pro Thr Xaa Lys Tyr Leu His Phe Leu Asp Phe Thr Phe Pro
85 90 95

Leu Xaa Ser Phe Lys Gln Asp Ser Xaa Asn Arg Lys Leu Val Xaa Ser
100 105 110

Pro Phe Arg Xaa Gln Lys Phe Trp Val Leu
115 120

<210> 614
<211> 62
<212> PRT
<213> Homo sapiens

<400> 614
Phe Phe Ile Gly Leu Glu Thr Arg Ala Asn Ser Ile Met Phe Ser Lys
1 5 10 15

Glu Thr Asp Leu Ser Cys Trp Ile Arg Gly Thr Asn Pro Thr Tyr Met
20 25 30

Ile Phe Phe Leu Phe Leu Ser Cys Ser Tyr Gly Thr Val Leu Phe Gly
35 40 45

Thr Phe Ala Thr Arg Asp Asn Thr Thr Phe Leu Thr Leu Ile
50 55 60

<210> 615
<211> 159
<212> PRT
<213> Homo sapiens

<400> 615
Val Gly Leu Pro Asn Met Ala Gln Ser Ile Asn Ile Thr Glu Leu Asn
1 5 10 15

Leu Pro Gln Leu Glu Met Leu Lys Asn Gln Leu Asp Gln Glu Val Glu
20 25 30

Phe Leu Ser Thr Ser Ile Ala Gln Leu Lys Val Val Gln Thr Lys Tyr
35 40 45

Val Glu Ala Lys Asp Cys Leu Asn Val Leu Asn Lys Ser Asn Glu Gly
50 55 60

Lys Glu Leu Leu Val Pro Leu Thr Ser Ser Met Tyr Val Pro Gly Lys
65 70 75 80

Leu His Asp Val Glu His Val Leu Ile Asp Val Gly Thr Gly Tyr Tyr
85 90 95

Val Glu Lys Thr Ala Glu Asp Ala Lys Asp Phe Phe Lys Arg Lys Ile
100 105 110

Asp Phe Leu Thr Lys Gln Met Glu Lys Ile Gln Pro Ala Leu Gln Glu
115 120 125

Lys His Ala Met Lys Gln Ala Val Met Glu Met Met Ser Gln Lys Ile
130 135 140

Gln Gln Leu Thr Ala Leu Gly Ala Ala Gln Ala Thr Ala Lys Ala
145 150 155

<210> 616
<211> 93
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 616
Lys Val Ala Cys Arg Tyr Arg Xaa Gly Ile Pro Gly Arg Pro Thr Arg
1 5 10 15

Pro Gly Thr Gln Asp Ala Glu Gly Lys Lys Ala Lys Gly Lys Lys Val
20 25 30

Ala Pro Ala Pro Ala Val Val Lys Lys Gln Glu Ala Lys Lys Val Val
35 40 45

Asn Pro Leu Phe Glu Lys Arg Pro Lys Asn Phe Gly Ile Gly Gln Asp
50 55 60

Ile Gln Pro Lys Arg Asp Leu Thr Arg Phe Val Lys Trp Pro Arg Tyr
65 70 75 80

Ile Arg Leu Gln Arg His Ala Arg Ser Ser Thr Ser Gly
85 90

<210> 617
<211> 362
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (307)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 617
Ser Arg Val Asp Pro Arg Val Arg Arg Gly Val Pro Tyr Gln Leu Gly
1 5 10 15

Pro His Gly His Arg Gln Gly Leu Glu Ala Pro Leu Tyr Leu Thr Pro
20 25 30

Glu Gly Trp Ser Leu Phe Leu Gln Arg Tyr Tyr Gln Val Val His Glu
35 40 45

Gly Ala Glu Leu Arg His Leu Asp Thr Gln Val Gln Arg Cys Glu Asp
50 55 60

Ile Leu Gln Gln Leu Gln Ala Val Val Pro Gln Ile Asp Met Glu Gly
65 70 75 80

Asp Arg Asn Ile Trp Ile Val Lys Pro Gly Ala Lys Ser Arg Gly Arg
85 90 95

Gly Ile Met Cys Met Asp His Leu Glu Glu Met Leu Lys Leu Val Asn
100 105 110

Gly Asn Pro Val Val Met Lys Asp Gly Lys Trp Val Val Gln Lys Tyr
115 120 125

Ile Glu Arg Pro Leu Leu Ile Phe Gly Thr Lys Phe Asp Leu Arg Gln
130 135 140

```
Trp Phe Leu Val Thr Asp Trp Asn Pro Leu Thr Val Trp Phe Tyr Arg
145                 150                 155                 160

Asp Ser Tyr Ile Arg Phe Ser Thr Gln Pro Phe Ser Leu Lys Asn Leu
                165                 170                 175

Asp Asn Ser Val His Leu Cys Asn Asn Ser Ile Gln Lys His Leu Glu
            180                 185                 190

Asn Ser Cys His Arg His Pro Leu Leu Pro Pro Asp Asn Met Trp Ser
        195                 200                 205

Ser Gln Arg Phe Gln Ala His Leu Gln Glu Met Gly Ala Pro Asn Ala
    210                 215                 220

Trp Ser Thr Ile Ile Val Pro Gly Met Lys Asp Ala Val Ile His Ala
225                 230                 235                 240

Leu Gln Thr Ser Gln Asp Thr Val Gln Cys Arg Lys Ala Ser Phe Glu
                245                 250                 255

Leu Tyr Gly Ala Asp Phe Val Phe Gly Glu Asp Phe Gln Pro Trp Leu
            260                 265                 270

Ile Glu Ile Asn Ala Ser Pro Thr Met Ala Pro Ser Thr Ala Val Thr
        275                 280                 285

Ala Arg Leu Cys Ala Gly Val Gln Ala Asp Thr Leu Arg Val Val Ile
    290                 295                 300

Asp Arg Xaa Leu Asp Arg Asn Cys Asp Thr Gly Ala Phe Glu Leu Ile
305                 310                 315                 320

Tyr Lys Gln Pro Ala Val Glu Val Pro Gln Tyr Val Gly Ile Arg Leu
                325                 330                 335

Leu Val Glu Gly Phe Thr Ile Lys Lys Pro Met Ala Met Cys His Arg
            340                 345                 350

Arg Met Gly Val Arg Gln Gln Ser Leu Cys
        355                 360
```

<210> 618
<211> 328
<212> PRT
<213> Homo sapiens

<400> 618

```
Ile Arg Met Arg Glu Trp Trp Val Gln Val Gly Leu Leu Ala Val Pro
 1               5                  10                  15

Leu Leu Ala Ala Tyr Leu His Ile Pro Pro Pro Gln Leu Ser Pro Ala
            20                  25                  30

Leu His Ser Trp Lys Ser Ser Gly Lys Phe Phe Thr Tyr Lys Gly Leu
        35                  40                  45

Arg Ile Phe Tyr Gln Asp Ser Val Gly Val Val Gly Ser Pro Glu Ile
    50                  55                  60

Val Val Leu Leu His Gly Phe Pro Thr Ser Ser Tyr Asp Trp Tyr Lys
65                  70                  75                  80

Ile Trp Glu Gly Leu Thr Leu Arg Phe His Arg Val Ile Ala Leu Asp
                85                  90                  95

Phe Leu Gly Phe Gly Phe Ser Asp Lys Pro Arg Pro His His Tyr Ser
            100                 105                 110

Ile Phe Glu Gln Ala Ser Ile Val Glu Ala Leu Leu Arg His Leu Gly
        115                 120                 125

Leu Gln Asn Arg Arg Ile Asn Leu Leu Ser His Asp Tyr Gly Asp Ile
    130                 135                 140

Val Ala Gln Glu Leu Leu Tyr Arg Tyr Lys Gln Asn Arg Ser Gly Arg
145                 150                 155                 160

Leu Thr Ile Lys Ser Leu Cys Leu Ser Asn Gly Gly Ile Phe Pro Glu
                165                 170                 175

Thr His Arg Pro Leu Leu Leu Gln Lys Leu Leu Lys Asp Gly Gly Val
            180                 185                 190

Leu Ser Pro Ile Leu Thr Arg Leu Met Asn Phe Phe Val Phe Ser Arg
        195                 200                 205

Gly Leu Thr Pro Val Phe Gly Pro Tyr Thr Arg Pro Ser Glu Ser Glu
    210                 215                 220

Leu Trp Asp Met Trp Ala Gly Ile Arg Asn Asn Asp Gly Asn Leu Val
225                 230                 235                 240

Ile Asp Ser Leu Leu Gln Tyr Ile Asn Gln Arg Lys Lys Phe Arg Arg
                245                 250                 255

Arg Trp Val Gly Ala Leu Ala Ser Val Thr Ile Pro Ile His Phe Ile
            260                 265                 270
```

Tyr Gly Pro Leu Asp Pro Val Asn Pro Tyr Pro Glu Phe Leu Glu Leu
275 280 285

Tyr Arg Lys Thr Leu Pro Arg Ser Thr Val Ser Ile Leu Asp Asp His
290 295 300

Ile Ser His Tyr Pro Gln Leu Glu Asp Pro Met Gly Phe Leu Asn Ala
305 310 315 320

Tyr Met Gly Phe Ile Asn Ser Phe
325

<210> 619
<211> 271
<212> PRT
<213> Homo sapiens

<400> 619
Asn Met Asp Pro Pro Gly Leu Gln Gly Val Gln Gly Thr Val Ala Ala
1 5 10 15

Cys Gly Ala Cys Tyr Trp Leu Leu Gly Leu Met Ala Val Arg Ala Ser
20 25 30

Phe Glu Asn Asn Cys Glu Ile Gly Cys Phe Ala Lys Leu Thr Asn Thr
35 40 45

Tyr Cys Leu Val Ala Ile Gly Gly Ser Glu Asn Phe Tyr Ser Val Phe
50 55 60

Glu Gly Glu Leu Ser Asp Thr Ile Pro Val Val His Ala Ser Ile Ala
65 70 75 80

Gly Cys Arg Ile Ile Gly Arg Met Cys Val Gly Asn Arg His Gly Leu
85 90 95

Leu Val Pro Asn Asn Thr Thr Asp Gln Glu Leu Gln His Ile Arg Asn
100 105 110

Ser Leu Pro Asp Thr Val Gln Ile Arg Arg Val Glu Glu Arg Leu Ser
115 120 125

Ala Leu Gly Asn Val Thr Thr Cys Asn Asp Tyr Val Ala Leu Val His
130 135 140

Pro Asp Leu Asp Arg Glu Thr Glu Glu Ile Leu Ala Asp Val Leu Lys
145 150 155 160

Val Glu Val Phe Arg Gln Thr Val Ala Asp Gln Val Leu Val Gly Ser

165 170 175

Tyr Cys Val Phe Ser Asn Gln Gly Gly Leu Val His Pro Lys Thr Ser
180 185 190

Ile Glu Asp Gln Asp Glu Leu Ser Ser Leu Leu Gln Val Pro Leu Val
195 200 205

Ala Gly Thr Val Asn Arg Gly Ser Glu Val Ile Ala Ala Gly Met Val
210 215 220

Val Asn Asp Trp Cys Ala Phe Cys Gly Leu Asp Thr Thr Ser Thr Glu
225 230 235 240

Leu Ser Val Val Glu Ser Val Phe Lys Leu Asn Glu Ala Gln Pro Ser
245 250 255

Thr Ile Ala Thr Ser Met Arg Asp Ser Leu Ile Asp Ser Leu Thr
260 265 270

<210> 620
<211> 88
<212> PRT
<213> Homo sapiens

<400> 620
Gly Ser Ala Ala Met Lys Val Lys Ile Lys Cys Trp Asn Gly Val Ala
1 5 10 15

Thr Trp Leu Trp Val Ala Asn Asp Glu Asn Cys Gly Ile Cys Arg Met
20 25 30

Ala Phe Asn Gly Cys Cys Pro Asp Cys Lys Val Pro Gly Asp Asp Cys
35 40 45

Pro Leu Val Trp Gly Gln Cys Ser His Cys Phe His Met His Cys Ile
50 55 60

Leu Lys Trp Leu His Ala Gln Gln Val Gln Gln His Cys Pro Met Cys
65 70 75 80

Arg Gln Glu Trp Lys Phe Lys Glu
85

<210> 621
<211> 46
<212> PRT

<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 621
Ala Gly Thr Ser Arg Ser Glu Gly Lys Arg Ser Ser Val Leu Thr Arg
1 5 10 15

Thr Glu Phe Gln Ile Glu Met Phe Gln Thr Ile Glu Gly Glu Lys Trp
20 25 30

Pro Gly Xaa Ser Ile Asn Leu Ser Xaa Phe His Gly Cys Phe
35 40 45

<210> 622
<211> 103
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (36)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 622
Gly Arg Pro Thr Arg Pro Arg Gly Arg Gly Arg Ser Ser Ala Cys Leu
1 5 10 15

Leu Leu Glu Gly Asp Gly Pro Ala Arg Leu Trp Ala Pro Thr Ser Pro
20 25 30

Gly Val Xaa Xaa Glu Arg Phe Ala Glu Glu Arg Gly Ser Gly Arg Ala
35 40 45

Leu Asn Ala Gly Pro Lys His Pro Gly Ser Leu His Ser Pro Arg Pro
50 55 60

Gln Thr Leu Thr Lys Thr Trp Ile Cys Ser Arg Phe Ser Cys Ser Arg
65 70 75 80

Ser Ser Arg Ser Cys Pro Arg Leu Leu Arg Leu Arg Ala Glu Lys Lys
85 90 95

Val Cys Gln Ala Trp Thr Gln
100

<210> 623
<211> 103
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (60)
<223> Xaa equals any of the naturally occurring-L-amino acids

<400> 623
Gly Arg Pro Thr Arg Pro Thr Ser Ser Arg Ser Arg Ala Ala Arg Pro
1 5 10 15

Phe Phe Phe Phe Phe Phe Phe Trp Phe Pro Glu Phe Gly Phe Ile Leu
20 25 30

Gln Tyr Arg Asn His Leu Glu Pro Ser Glu Thr Asp Ile Pro Glu Ala
35 40 45

Glu Ala Leu Ser Asn Gln Tyr Cys Val Ala Leu Xaa Pro Leu Arg Lys
50 55 60

Pro His Leu Gly Tyr Lys Arg Ser Phe Tyr Val Tyr Pro Leu Tyr His
65 70 75 80

Gly Phe Leu Ser Pro Leu Leu Leu Pro Ile Leu Pro Gly Glu Asn Thr
85 90 95

Ala Gln Arg Leu Pro Ser Glu
100

<210> 624
<211> 305
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (116)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (117)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (219)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 624
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Thr Gln Asp Leu Trp Met Ser Cys Pro Val Gln Thr Met Asp Pro Glu
  1               5                  10                  15

Val Thr Leu Leu Leu Gln Cys Pro Gly Gly Gly Leu Pro Gln Glu Gln
             20                  25                  30

Ile Gln Ala Glu Leu Ser Pro Ala His Asp Arg Arg Pro Leu Pro Gly
         35                  40                  45

Gly Asp Glu Ala Ile Thr Ala Ile Trp Glu Thr Arg Leu Lys Ala Gln
     50                  55                  60

Pro Trp Leu Phe Asp Ala Pro Lys Phe Arg Leu His Ser Ala Thr Leu
 65                  70                  75                  80

Ala Pro Ile Gly Ser Arg Gly Pro Gln Leu Leu Leu Arg Leu Gly Leu
                 85                  90                  95

Thr Ser Tyr Arg Asp Phe Leu Gly Thr Asn Trp Ser Ser Ser Ala Ala
            100                 105                 110

Trp Leu Arg Xaa Xaa Gly Ala Thr Asp Trp Gly Asp Thr Gln Ala Tyr
        115                 120                 125

Leu Ala Asp Pro Leu Gly Val Gly Ala Ala Leu Ala Thr Ala Asp Asp
    130                 135                 140

Phe Leu Val Phe Leu Arg Arg Ser Arg Gln Val Ala Glu Ala Pro Gly
145                 150                 155                 160

Leu Val Asp Val Pro Gly Gly His Pro Glu Pro Gln Ala Leu Cys Pro
                165                 170                 175

Gly Gly Ser Pro Gln His Gln Asp Leu Ala Gly Gln Leu Val Val His
            180                 185                 190
```

Glu Leu Phe Ser Ser Val Leu Gln Glu Ile Cys Asp Glu Val Asn Leu
195 200 205

Pro Leu Leu Thr Leu Ser Gln Pro Leu Leu Xaa Gly Ile Ala Arg Asn
210 215 220

Glu Thr Ser Ala Gly Arg Ala Ser Ala Glu Phe Tyr Val Gln Cys Ser
225 230 235 240

Leu Thr Ser Glu Gln Val Arg Lys His Tyr Leu Ser Gly Gly Pro Glu
245 250 255

Ala His Glu Ser Thr Gly Ile Phe Phe Val Glu Thr Gln Asn Val Arg
260 265 270

Arg Leu Pro Glu Thr Glu Met Trp Ala Glu Leu Cys Pro Ser Pro Lys
275 280 285

Ala Pro Ser Ser Ser Thr Thr Gly Phe Arg Glu Val Pro Leu Glu Arg
290 295 300

Pro
305

<210> 625
<211> 102
<212> PRT
<213> Homo sapiens

<400> 625
Ser Ala Met Lys Ala Ser Gly Thr Leu Arg Glu Tyr Lys Val Val Gly
1 5 10 15

Arg Cys Leu Pro Thr Pro Lys Cys Arg Thr Pro Pro Leu Tyr Arg Met
20 25 30

Arg Ile Phe Ala Pro Asn His Val Val Ala Lys Ser Arg Phe Trp Tyr
35 40 45

Phe Val Ser Gln Leu Lys Lys Met Lys Lys Ser Ser Gly Glu Ile Val
50 55 60

Tyr Cys Gly Gln Val Phe Glu Lys Ser Pro Leu Arg Val Lys Asn Phe
65 70 75 80

Gly Ile Trp Leu Arg Tyr Asp Ser Arg Ser Gly Thr His Asn Met Tyr
85 90 95

Arg Gly Val Pro Gly Thr
100

<210> 626
<211> 59
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (36)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 626
Ala Leu Trp Val Lys Ala Trp Arg Gln Glu Ser Glu Gly Gln Phe Gln
1 5 10 15

Glu Thr Gln Phe Ile Asn Phe His Gln His Leu Pro Gly Pro Cys Leu
20 25 30

Gly Thr Glu Xaa Pro Ser Pro Glu Ser Gly His His Phe Pro Phe Gln
35 40 45

Ser Ile Glu Cys Arg Gly Ile Gln Gly Met Gly
50 55

<210> 627
<211> 220
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (93)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 627
Arg Leu Val Val Thr Glu Glu Asp Gly Gly Ala Arg Pro Glu Ala Leu
1 5 10 15

Gly Lys Ile Ala Pro Arg Thr Pro Ala Glu Leu Gly Ala Arg Ala Asp
20 25 30

Gln Glu Leu Val Thr Ala Leu Met Cys Asp Leu Arg Arg Pro Ala Ala
35 40 45

Gly Gly Met Met Asp Leu Ala Tyr Val Cys Glu Trp Glu Lys Trp Ser

```
     50                  55                  60

Lys Ser Thr His Cys Pro Ser Val Pro Leu Ala Cys Ala Trp Ser Cys
 65                  70                  75                  80

Arg Asn Leu Ile Ala Phe Thr Met Asp Leu Arg Thr Xaa Asp Gln Asp
                85                  90                  95

Leu Thr Arg Met Ile His Ile Leu Asp Thr Glu His Pro Trp Asp Leu
            100                 105                 110

His Ser Ile Pro Ser Glu His His Glu Ala Ile Thr Cys Leu Glu Trp
        115                 120                 125

Asp Gln Ser Gly Ser Arg Leu Leu Ser Ala Asp Ala Asp Gly Gln Ile
    130                 135                 140

Lys Cys Trp Ser Met Ala Asp His Leu Ala Asn Ser Trp Glu Ser Ser
145                 150                 155                 160

Val Gly Ser Leu Val Glu Gly Asp Pro Ile Val Ala Leu Ser Trp Leu
                165                 170                 175

His Asn Gly Val Lys Leu Ala Leu His Val Glu Lys Ser Gly Ala Ser
            180                 185                 190

Ser Phe Gly Glu Lys Phe Ser Arg Val Lys Phe Ser Pro Val Leu Thr
        195                 200                 205

Leu Phe Gly Gly Lys Pro Trp Arg Ala Gly Ser Arg
    210                 215                 220
```

<210> 628
<211> 119
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (117)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 628
Pro Ala Ser Val Glu Val Tyr His Asp Ser Leu Cys Arg Lys Ile Trp

```
 1               5                   10                  15

Arg Glu Asp Asp Lys Trp His Val Ile Phe Arg Ala Asp Gly Trp Glu
            20                  25                  30

Gln His Ile Thr Ala Arg Tyr Leu Val Gly Ala Asp Gly Ala Asn Ser
        35                  40                  45

Met Val Arg Arg His Leu Tyr Pro Asp His Gln Ile Arg Lys Tyr Val
    50                  55                  60

Ala Ile Gln Gln Trp Phe Ala Glu Lys His Pro Val Pro Phe Tyr Ser
65                  70                  75                  80

Cys Ile Phe Asp Asn Ser Ile Thr Asn Cys Tyr Ser Trp Ser Ile Ser
                85                  90                  95

Lys Asp Gly Tyr Phe Ile Phe Gly Gly Ala Tyr Pro Met Glu Arg Arg
            100                 105                 110

Ser Asp Xaa Phe Xaa Asp Ala
        115
```

<210> 629
<211> 39
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 629

```
Phe Gly Glu Pro Ser Leu Thr Val Arg Ala Asp Ile Thr Gly Arg Tyr
 1               5                   10                  15

Ser Ile Val Ser Met Leu Thr Thr Cys Arg Tyr Ser Leu Xaa Xaa His
            20                  25                  30

Met Lys Lys Val Ser Ser Cys
        35
```

<210> 630
<211> 267
<212> PRT
<213> Homo sapiens

<400> 630
Ser Ala Ala Leu Pro Gln Pro Thr Pro Pro Leu Thr Leu Pro Gln Ser
1   5   10   15

Met Val Asn Thr Lys Pro Glu Lys Thr Glu Glu Asp Ser Glu Glu Val
            20   25   30

Arg Glu Gln Lys His Lys Thr Phe Val Glu Lys Tyr Glu Lys Gln Ile
        35   40   45

Lys His Phe Gly Met Leu Arg Arg Trp Asp Asp Ser Gln Lys Tyr Leu
    50   55   60

Ser Asp Asn Val His Leu Val Cys Glu Glu Thr Ala Asn Tyr Leu Val
65   70   75   80

Ile Trp Cys Ile Asp Leu Glu Val Glu Glu Lys Cys Ala Leu Met Glu
                85   90   95

Gln Val Ala His Gln Thr Ile Val Met Gln Phe Ile Leu Glu Leu Ala
            100   105   110

Lys Ser Leu Lys Val Asp Pro Arg Ala Cys Phe Arg Gln Phe Phe Thr
        115   120   125

Lys Ile Lys Thr Ala Asp Arg Gln Tyr Met Glu Gly Phe Asn Asp Glu
    130   135   140

Leu Glu Ala Phe Lys Glu Arg Val Arg Gly Arg Ala Lys Leu Arg Ile
145   150   155   160

Glu Lys Ala Met Lys Glu Tyr Glu Glu Glu Glu Arg Lys Lys Arg Leu
                165   170   175

Gly Pro Gly Gly Leu Asp Pro Val Glu Val Tyr Glu Ser Leu Pro Glu
            180   185   190

Glu Leu Gln Lys Cys Phe Asp Val Lys Asp Val Gln Met Leu Gln Asp
        195   200   205

Ala Ile Ser Lys Met Asp Pro Thr Asp Ala Lys Tyr His Met Gln Arg
    210   215   220

Cys Ile Asp Ser Gly Leu Trp Val Pro Asn Ser Lys Ala Ser Glu Ala
225   230   235   240

```
Lys Glu Gly Glu Glu Ala Gly Pro Gly Asp Pro Leu Leu Glu Ala Val
                245                 250                 255

Pro Lys Thr Gly Asp Glu Lys Asp Val Ser Val
            260                 265



<210> 631
<211> 207
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (164)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 631
Pro Thr Gly Thr Gly Ser Gly Val Pro Gly Leu Gly Arg Asn Gly Gly
  1               5                  10                  15

Arg Glu Gly Ala Pro Gly Thr Met Gly Leu Leu Thr Ile Leu Lys Lys
             20                  25                  30

Met Lys Gln Lys Glu Arg Glu Leu Arg Leu Leu Met Leu Gly Leu Asp
         35                  40                  45

Asn Ala Gly Lys Thr Thr Ile Leu Lys Lys Phe Asn Gly Glu Asp Ile
     50                  55                  60

Asp Thr Ile Ser Pro Thr Leu Gly Phe Asn Ile Lys Thr Leu Glu His
 65                  70                  75                  80

Arg Gly Phe Lys Leu Asn Ile Trp Asp Val Gly Gly Gln Lys Ser Leu
                 85                  90                  95

Arg Ser Tyr Trp Arg Asn Tyr Phe Glu Ser Thr Asp Gly Leu Ile Trp
            100                 105                 110

Val Val Asp Ser Ala Asp Arg Gln Arg Met Gln Asp Cys Gln Arg Glu
        115                 120                 125

Leu Gln Ser Leu Leu Val Glu Glu Arg Leu Ala Gly Ala Thr Leu Leu
    130                 135                 140

Ile Phe Ala Asn Lys Gln Asp Leu Pro Gly Ala Leu Ser Ser Asn Ala
145                 150                 155                 160

Ile Arg Glu Xaa Leu Glu Leu Asp Ser Ile Arg Ser His His Trp Cys
```

165 170 175

Ile Gln Gly Cys Ser Ala Val Thr Gly Glu Asn Leu Leu Pro Gly Ile
180 185 190

Asp Trp Leu Leu Asp Asp Ile Ser Ser Arg Ile Phe Thr Ala Asp
195 200 205

<210> 632
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (60)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (61)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (73)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 632
Lys Asn Asn Lys Lys Asp Gln Gln Asn Gly Ile Cys Ser His Thr Met
1 5 10 15

Ile Lys Thr Tyr Leu Arg Thr Ala Leu Phe Met Gly Lys Arg Ser Leu
20 25 30

Ile Asp Ser Gln Phe His Arg Leu Tyr Arg Arg His Gly Leu Gly Arg
35 40 45

Pro Gln Gly Asn Leu Xaa Ser Met Val Glu Gly Xaa Xaa Gly Ser Met
50 55 60

His His Leu His Trp Pro Glu Gln Xaa Glu Arg Glu Gln Ile Trp
65 70 75

<210> 633
<211> 293
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (249)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (282)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 633
Trp Ser Pro Ser Pro Pro Ala Thr Pro Glu Gln Gly Leu Ser Ala Phe
1 5 10 15

Tyr Leu Ser Tyr Phe Asp Met Leu Tyr Pro Glu Asp Ser Ser Trp Ala
20 25 30

Ala Lys Ala Pro Gly Ala Ser Ser Arg Glu Glu Pro Pro Glu Glu Pro
35 40 45

Glu Gln Cys Pro Val Ile Asp Ser Gln Ala Pro Ala Gly Ser Leu Asp
50 55 60

Leu Val Pro Gly Gly Leu Thr Leu Glu Glu His Ser Leu Glu Gln Val
65 70 75 80

Gln Ser Met Val Val Gly Glu Val Leu Lys Asp Ile Glu Thr Ala Cys
85 90 95

Lys Leu Leu Asn Ile Thr Ala Asp Pro Met Asp Trp Ser Pro Ser Asn
100 105 110

Val Gln Lys Trp Leu Leu Trp Thr Glu His Gln Tyr Arg Leu Pro Pro
115 120 125

Met Gly Lys Ala Phe Gln Glu Leu Ala Gly Lys Glu Leu Cys Ala Met
130 135 140

Ser Glu Glu Gln Phe Arg Gln Arg Ser Pro Leu Gly Gly Asp Val Leu
145 150 155 160

His Ala His Leu Asp Ile Trp Lys Ser Ala Ala Trp Met Lys Glu Arg
165 170 175

Thr Ser Pro Gly Ala Ile His Tyr Cys Ala Ser Thr Ser Glu Glu Ser
180 185 190

Trp Thr Asp Ser Glu Val Asp Ser Ser Cys Ser Gly Gln Pro Ile His
195 200 205

Leu Trp Gln Phe Leu Lys Glu Leu Leu Leu Lys Pro His Ser Tyr Gly
210 215 220

Arg Phe Ile Arg Trp Leu Asn Lys Glu Lys Gly Ile Phe Lys Ile Glu
225 230 235 240

Asp Ser Ala Gln Val Ala Arg Leu Xaa Gly Ile Arg Lys Asn Arg Pro
245 250 255

Ala Met Asn Tyr Asp Lys Leu Ser Arg Ser Ile Arg Gln Tyr Tyr Lys
260 265 270

Lys Gly Ile Ile Arg Lys Pro Asp Ile Xaa Gln Arg Leu Val Tyr Gln
275 280 285

Phe Val His Pro Ile
290

<210> 634
<211> 227
<212> PRT
<213> Homo sapiens

<400> 634
Pro Ala Gly Thr Gly Pro Glu Phe Pro Gly Arg Pro Thr Arg Pro Ala
1 5 10 15

Glu Glu Glu Glu Glu Glu Asp Glu Glu Glu Glu Glu Glu Glu Glu Glu
20 25 30

Glu Glu Glu Glu Glu Pro Gln Gln Arg Gly Gln Gly Glu Lys Ser Ala
35 40 45

Thr Pro Ser Arg Lys Ile Leu Asp Pro Asn Thr Gly Glu Pro Ala Pro
50 55 60

Val Leu Ser Ser Pro Pro Pro Ala Asp Val Ser Thr Phe Leu Ala Phe
65 70 75 80

Pro Ser Pro Glu Lys Leu Leu Arg Leu Gly Pro Lys Ser Ser Val Leu
85 90 95

Ile Ala Gln Gln Thr Asp Thr Ser Asp Pro Glu Lys Val Val Ser Ala

```
            100                 105                 110

Phe Leu Lys Val Ser Ser Val Phe Lys Asp Glu Ala Thr Val Arg Met
        115                 120                 125

Ala Val Gln Asp Ala Val Asp Ala Leu Met Gln Lys Ala Phe Asn Ser
    130                 135                 140

Ser Ser Phe Asn Ser Asn Thr Phe Leu Thr Arg Leu Leu Val His Met
145                 150                 155                 160

Gly Leu Leu Lys Ser Glu Asp Lys Val Lys Ala Ile Ala Asn Leu Tyr
                165                 170                 175

Gly Pro Leu Met Ala Leu Asn His Met Val Gln Gln Asp Tyr Phe Pro
            180                 185                 190

Lys Ala Leu Ala Pro Leu Leu Leu Ala Phe Val Thr Lys Pro Asn Ser
        195                 200                 205

Ala Leu Glu Ser Cys Ser Phe Ala Arg His Ser Leu Leu Gln Thr Leu
    210                 215                 220

Tyr Lys Val
225



<210> 635
<211> 126
<212> PRT
<213> Homo sapiens

<400> 635
Thr Ser Gly Cys Ile Ser Asn Gly Lys Met Ser Ser Asn Val Pro Ala
  1               5                  10                  15

Asp Met Ile Asn Leu Arg Leu Ile Leu Val Ser Gly Lys Thr Lys Glu
             20                  25                  30

Phe Leu Phe Ser Pro Asn Asp Ser Ala Ser Asp Ile Ala Lys His Val
         35                  40                  45

Tyr Asp Asn Trp Pro Met Asp Trp Glu Glu Glu Gln Val Ser Ser Pro
     50                  55                  60

Asn Ile Leu Arg Leu Ile Tyr Gln Gly Arg Phe Leu His Gly Asn Val
 65                  70                  75                  80

Thr Leu Gly Ala Leu Lys Leu Pro Phe Gly Lys Thr Thr Val Met His
                 85                  90                  95
```

```
Leu Val Ala Arg Glu Thr Leu Pro Glu Pro Asn Ser Gln Gly Gln Arg
            100                 105                 110

Asn Arg Glu Lys Thr Gly Glu Ser Asn Cys Cys Val Ile Leu
        115                 120                 125



<210> 636
<211> 195
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (96)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 636
Val Ser Gly Phe Ala Gly Pro Ala Ser Leu Ile Ser Met Lys Leu Leu
  1               5                  10                  15

Ser Leu Val Ala Val Val Gly Cys Leu Leu Val Pro Pro Ala Glu Ala
             20                  25                  30

Asn Lys Ser Ser Glu Asp Ile Arg Cys Lys Cys Ile Cys Pro Pro Tyr
         35                  40                  45

Arg Asn Ile Ser Gly His Ile Tyr Asn Gln Asn Val Ser Gln Lys Asp
     50                  55                  60

Cys Asn Cys Leu His Val Val Glu Pro Met Pro Val Pro Gly His Asp
 65                  70                  75                  80

Val Glu Ala Tyr Cys Leu Leu Cys Glu Cys Arg Tyr Glu Glu Arg Xaa
                 85                  90                  95

Thr Thr Thr Ile Lys Val Ile Ile Val Ile Tyr Leu Ser Val Val Gly
            100                 105                 110

Ala Leu Leu Leu Tyr Met Ala Phe Leu Met Leu Val Asp Pro Leu Ile
        115                 120                 125

Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His Asn Glu Glu Glu Asn
    130                 135                 140

Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Ser Leu Gly Gly Pro
145                 150                 155                 160

Arg Ala Asn Thr Val Leu Glu Arg Val Glu Gly Ala Gln Gln Arg Trp
```

165 170 175

Lys Leu Gln Val Gln Glu Gln Arg Lys Thr Val Phe Asp Arg His Lys
180 185 190

Met Leu Ser
195

<210> 637
<211> 159
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (92)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (138)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (151)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (156)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 637
Arg Pro Thr Arg Pro Gly Asn Ser Arg Arg Arg Gly Arg Arg Gly Cys
1 5 10 15

Trp Arg Leu Leu Gly Phe Gly Ala Ala Ala Ile Met Pro Gly Ile Val
20 25 30

Glu Leu Pro Thr Leu Glu Asp Leu Lys Val Gln Glu Val Lys Val Ser
35 40 45

Ser Ser Val Leu Lys Ala Ala Ala His His Tyr Gly Val Gln Cys Asp

50 55 60

Lys Pro Asn Lys Glu Phe Met Leu Cys Arg Trp Glu Glu Lys Asp Pro
65 70 75 80

Arg Arg Cys Leu Glu Glu Gly Lys Leu Val Asn Xaa Cys Ala Leu Asp
85 90 95

Phe Phe Arg Gln Ile Lys Leu Ser Leu Cys Arg Ala Phe Tyr Arg Leu
100 105 110

Leu Asp Xaa His Arg Leu Leu Arg Pro Ala Val Phe Ser Ser Leu Pro
115 120 125

Gln Thr Ala Gly Gln Phe Asp Asp Val Xaa Gly Ala Thr Gly Met Val
130 135 140

Arg Leu Asn Trp Gly Lys Xaa Ser Ser His Gln Xaa Glu Asn Ser
145 150 155

<210> 638
<211> 20
<212> PRT
<213> Homo sapiens

<400> 638
Phe Ser Arg Asp Lys Val Ser Pro Cys Trp Pro Gly Trp Ser Arg Thr
1 5 10 15

Pro Gly Leu Arg
20

<210> 639
<211> 408
<212> PRT
<213> Homo sapiens

<400> 639
Thr Trp Gly Gln Thr Pro Cys Ser Pro Gly His Gly Gln Arg Pro Ser
1 5 10 15

Ser Thr Cys Leu Thr Val Gly Pro Gly Gly Gly Pro Ser Leu Gly Arg
20 25 30

Pro Cys Pro Gln Leu Leu Leu Gln Phe Gly Val Leu Phe Cys Thr Ile
35 40 45

```
Leu Leu Leu Leu Trp Val Ser Val Phe Leu Tyr Gly Ser Phe Tyr Tyr
     50                  55                  60

Ser Tyr Met Pro Thr Val Ser His Leu Ser Pro Val His Phe Tyr Tyr
 65                  70                  75                  80

Arg Thr Asp Cys Asp Ser Ser Thr Thr Ser Leu Cys Ser Phe Pro Val
                 85                  90                  95

Ala Asn Val Ser Leu Thr Lys Gly Gly Arg Asp Arg Val Leu Met Tyr
            100                 105                 110

Gly Gln Pro Tyr Arg Val Thr Leu Glu Leu Glu Leu Pro Glu Ser Pro
        115                 120                 125

Val Asn Gln Asp Leu Gly Met Phe Leu Val Thr Ile Ser Cys Tyr Thr
    130                 135                 140

Arg Gly Gly Arg Ile Ile Ser Thr Ser Ser Arg Ser Val Met Leu His
145                 150                 155                 160

Tyr Arg Ser Asp Leu Leu Gln Met Leu Asp Thr Leu Val Phe Ser Ser
                165                 170                 175

Leu Leu Leu Phe Gly Phe Ala Glu Gln Lys Gln Leu Leu Glu Val Glu
            180                 185                 190

Leu Tyr Ala Asp Tyr Arg Glu Asn Ser Tyr Val Pro Thr Thr Gly Ala
        195                 200                 205

Ile Ile Glu Ile His Ser Lys Arg Ile Gln Leu Tyr Gly Ala Tyr Leu
    210                 215                 220

Arg Ile His Ala His Phe Thr Gly Leu Arg Tyr Leu Leu Tyr Asn Phe
225                 230                 235                 240

Pro Met Thr Cys Ala Phe Ile Gly Val Ala Ser Asn Phe Thr Phe Leu
                245                 250                 255

Ser Val Ile Val Leu Phe Ser Tyr Met Gln Trp Val Trp Gly Gly Ile
            260                 265                 270

Trp Pro Arg His Arg Phe Ser Leu Gln Val Asn Ile Arg Lys Arg Asp
        275                 280                 285

Asn Ser Arg Lys Glu Val Gln Arg Arg Ile Ser Ala His Gln Pro Gly
    290                 295                 300

Pro Glu Gly Gln Glu Glu Ser Thr Pro Gln Ser Asp Val Thr Glu Asp
305                 310                 315                 320
```

```
Gly Glu Ser Pro Glu Asp Pro Ser Gly Thr Glu Gly Gln Leu Ser Glu
                325                 330                 335

Glu Glu Lys Pro Asp Gln Gln Pro Leu Ser Gly Glu Glu Glu Leu Glu
            340                 345                 350

Pro Glu Ala Ser Asp Gly Ser Gly Ser Trp Glu Asp Ala Ala Leu Leu
        355                 360                 365

Thr Glu Ala Asn Leu Pro Ala Pro Ala Pro Ala Ser Ala Ser Ala Pro
    370                 375                 380

Val Leu Glu Thr Leu Gly Ser Ser Glu Pro Ala Gly Gly Ala Leu Arg
385                 390                 395                 400

Gln Arg Pro Thr Cys Ser Ser Ser
                405
```

<210> 640
<211> 288
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (268)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (271)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (273)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (274)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (276)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (286)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 640

```
Phe Ser Ser Ser Ala Cys Pro Ser Val Xaa Ser Leu Phe Val Xaa Leu
  1               5                  10                  15

Gly Lys Asn Pro His Asp Ala Gln Gly His Pro Arg Ala Ser Glu Asp
             20                  25                  30

Gln Pro Ser Ser Gly Lys Pro Val Thr Ser Tyr Pro Gly Glu Cys Gly
         35                  40                  45

Phe Val Phe Thr Lys Glu Ala Ser Leu Glu Ile Arg Asp Met Leu Leu
     50                  55                  60

Ala Asn Lys Val Pro Ala Ala Ala Arg Ala Gly Ala Ile Ala Pro Cys
 65                  70                  75                  80

Glu Val Thr Val Pro Ala Gln Asn Thr Gly Leu Gly Pro Glu Lys Thr
                 85                  90                  95

Ser Phe Phe Gln Ala Leu Gly Ile Thr Thr Lys Ile Ser Arg Gly Thr
            100                 105                 110

Ile Glu Ile Leu Ser Asp Val Gln Leu Ile Lys Thr Gly Asp Lys Val
        115                 120                 125

Gly Ala Ser Glu Ala Thr Leu Leu Asn Met Leu Asn Ile Ser Pro Phe
    130                 135                 140

Ser Phe Gly Leu Ile Ile Gln Gln Val Phe Asp Asn Gly Ser Ile Tyr
145                 150                 155                 160

Asn Pro Glu Val Leu Asp Ile Thr Glu Glu Thr Leu His Ser Arg Phe
                165                 170                 175

Leu Glu Gly Val Arg Asn Val Ala Ser Val Cys Leu Gln Ile Gly Tyr
            180                 185                 190
```

Pro Thr Val Ala Ser Val Pro His Ser Ile Ile Asn Gly Tyr Lys Arg
195 200 205

Val Leu Ala Leu Ser Val Glu Thr Asp Tyr Thr Phe Pro Leu Ala Glu
210 215 220

Lys Val Lys Ala Phe Leu Ala Asp Pro Ser Ala Phe Val Ala Ala Ala
225 230 235 240

Pro Val Ala Ala Ala Thr Thr Ala Ala Pro Ala Ala Ala Ala Ala Pro
245 250 255

Ala Lys Val Glu Ala Lys Glu Glu Ser Glu Glu Xaa Asp Glu Xaa Ile
260 265 270

Xaa Xaa Ser Xaa Ile Ser Lys Ser Asn Asn Ser Ser Gln Xaa Ile Val
275 280 285

<210> 641
<211> 444
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (34)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 641
Asn Glu Gln Asp Asn Cys Val Leu Ile His Asp Val Asp Gln Arg Asn
1 5 10 15

Ser Asp Lys Asp Ile Phe Gly Asp Ala Cys Asp Asn Cys Leu Ser Val
20 25 30

Leu Xaa Asn Asp Gln Lys Asp Thr Asp Gly Asp Gly Arg Gly Asp Ala
35 40 45

Cys Asp Asp Asp Met Asp Gly Asp Gly Ile Lys Asn Ile Leu Asp Asn
50 55 60

Cys Pro Lys Phe Pro Asn Arg Asp Gln Arg Asp Lys Asp Gly Asp Gly
65 70 75 80

Val Gly Asp Ala Cys Asp Ser Cys Pro Asp Val Ser Asn Pro Asn Gln
85 90 95

Ser Asp Val Asp Asn Asp Leu Val Gly Asp Ser Cys Asp Thr Asn Gln
100 105 110

Asp Ser Asp Gly Asp Gly His Gln Asp Ser Thr Asp Asn Cys Pro Thr
115 120 125

Val Ile Asn Ser Ala Gln Leu Asp Thr Asp Lys Asp Gly Ile Gly Asp
130 135 140

Glu Cys Asp Asp Asp Asp Asp Asn Asp Gly Ile Pro Asp Leu Val Pro
145 150 155 160

Pro Gly Pro Asp Asn Cys Arg Leu Val Pro Asn Pro Ala Gln Glu Asp
165 170 175

Ser Asn Ser Asp Gly Val Gly Asp Ile Cys Glu Ser Asp Phe Asp Gln
180 185 190

Asp Gln Val Ile Asp Arg Ile Asp Val Cys Pro Glu Asn Ala Glu Val
195 200 205

Thr Leu Thr Asp Phe Arg Ala Tyr Gln Thr Val Val Leu Asp Pro Glu
210 215 220

Gly Asp Ala Gln Ile Asp Pro Asn Trp Val Val Leu Asn Gln Gly Met
225 230 235 240

Glu Ile Val Gln Thr Met Asn Ser Asp Pro Gly Leu Ala Val Gly Tyr
245 250 255

Thr Ala Phe Asn Gly Val Asp Phe Glu Gly Thr Phe His Val Asn Thr
260 265 270

Gln Thr Asp Asp Asp Tyr Ala Gly Phe Ile Phe Gly Tyr Gln Asp Ser
275 280 285

Ser Ser Phe Tyr Val Val Met Trp Lys Gln Thr Glu Gln Thr Tyr Trp
290 295 300

Gln Ala Thr Pro Phe Arg Ala Val Ala Glu Pro Gly Ile Gln Leu Lys
305 310 315 320

Ala Val Lys Ser Lys Thr Gly Pro Gly Glu His Leu Arg Asn Ser Leu
325 330 335

Trp His Thr Gly Asp Thr Ser Asp Gln Val Arg Leu Leu Trp Lys Asp
340 345 350

Ser Arg Asn Val Gly Trp Lys Asp Lys Val Ser Tyr Arg Trp Phe Leu
355 360 365

```
Gln His Arg Pro Gln Val Gly Tyr Ile Arg Val Arg Phe Tyr Glu Gly
    370                 375                 380

Ser Glu Leu Val Ala Asp Ser Gly Val Thr Ile Asp Thr Thr Met Arg
385                 390                 395                 400

Gly Gly Arg Leu Gly Val Phe Cys Phe Ser Gln Glu Asn Ile Ile Trp
                405                 410                 415

Ser Asn Leu Lys Tyr Arg Cys Asn Asp Thr Ile Pro Glu Asp Phe Gln
            420                 425                 430

Glu Phe Gln Thr Gln Asn Phe Asp Arg Phe Asp Asn
        435                 440



<210> 642
<211> 326
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (50)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (296)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 642
Ser Ala Arg Ala Ser Asp Leu Gly Ala Pro Arg Thr Trp Thr Gly Ala
  1               5                  10                  15

Ala Ala Gly Pro Arg Thr Pro Ser Ala His Ile Pro Val Pro Ala Gln
            20                  25                  30

Arg Ala Thr Pro Gly Lys Ala Arg Leu Asp Glu Val Met Ala Ala Ala
        35                  40                  45

Ala Xaa Thr Ser Leu Ser Thr Ser Pro Leu Leu Leu Gly Ala Pro Val
     50                  55                  60

Ala Ala Phe Ser Pro Glu Pro Gly Leu Glu Pro Trp Lys Glu Ala Leu
 65                  70                  75                  80

Val Arg Pro Pro Gly Ser Tyr Ser Ser Ser Ser Asn Ser Gly Asp Trp
                 85                  90                  95
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Gly Trp Asp Leu Ala Ser Asp Gln Ser Ser Pro Ser Thr Pro Ser Pro
            100                 105                 110

Pro Leu Pro Pro Glu Ala Ala His Phe Leu Phe Gly Glu Pro Thr Leu
        115                 120                 125

Arg Lys Arg Lys Ser Pro Ala Gln Val Met Phe Gln Cys Leu Trp Lys
    130                 135                 140

Ser Cys Gly Lys Val Leu Ser Thr Ala Ser Ala Met Gln Arg His Ile
145                 150                 155                 160

Arg Leu Val His Leu Gly Arg Gln Ala Glu Pro Asp Gln Ser Asp Gly
                165                 170                 175

Glu Glu Asp Phe Tyr Tyr Thr Glu Leu Asp Val Gly Val Asp Thr Leu
            180                 185                 190

Thr Asp Gly Leu Ser Ser Leu Thr Pro Val Ser Pro Thr Ala Ser Met
        195                 200                 205

Pro Pro Ala Phe Pro Arg Leu Glu Leu Pro Glu Leu Leu Glu Pro Pro
    210                 215                 220

Ala Leu Pro Ser Pro Leu Arg Pro Pro Ala Pro Pro Leu Pro Pro Pro
225                 230                 235                 240

Pro Val Leu Ser Thr Val Ala Asn Pro Gln Ser Cys His Ser Asp Arg
                245                 250                 255

Val Tyr Gln Gly Cys Leu Thr Pro Ala Arg Leu Glu Pro Gln Pro Thr
            260                 265                 270

Glu Val Gly Ala Cys Pro Pro Ala Leu Ser Ser Arg Ile Gly Val Thr
        275                 280                 285

Leu Arg Lys Pro Arg Gly Asp Xaa Lys Lys Cys Arg Lys Val Tyr Gly
    290                 295                 300

Met Glu Arg Arg Asp Leu Trp Cys Thr Ala Cys Arg Trp Lys Lys Ala
305                 310                 315                 320

Cys Gln Arg Phe Leu Asp
                325
```

<210> 643
<211> 129
<212> PRT

<213> Homo sapiens

<220>
<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (14)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (19)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (24)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (94)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (103)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 643
Asp Val Arg Leu Ser Gly Arg Asn Xaa Xaa Val Asp Val Xaa Asp His
1 5 10 15

Gln Xaa Xaa Leu Leu Glu Gln Xaa Asp Leu Leu Ala Gly Leu Ile Ser
20 25 30

Asn Ser Ser Asp Ala Xaa Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp
35 40 45

Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Leu Ile Pro
50 55 60

Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Gly Tyr Arg Asp Arg Met
65 70 75 80

Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Xaa Ser Gly
85 90 95

Thr Lys Ala Phe Met Glu Xaa Leu Gln Ala Gly Ala Asp Ile Ser Met
100 105 110

Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Arg
115 120 125

Arg

<210> 644
<211> 156
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 644
Ser Thr His Ala Ser Ala Ser Arg Arg Leu Leu Xaa Asp Val Cys Gln
1 5 10 15

Asp Cys Ile Gln Met Val Thr Asp Ile Gln Thr Ala Val Arg Thr Asn
20 25 30

Ser Thr Phe Val Glu Ala Leu Val Asp His Ala Lys Ala Gln Cys Asp
35 40 45

Leu Leu Gly Pro Gly Met Ala Asp Met Cys Lys Asn Tyr Ile Asn Gln
50 55 60

Tyr Ser Asp Ile Ala Val Gln Met Met Met His Met Gln Pro Lys Glu
65 70 75 80

Ile Cys Gly Leu Val Gly Phe Cys Asp Gln Val Lys Glu Met Pro Met
85 90 95

Gln Thr Leu Ile Pro Ala Lys Ala Val Ser Glu Asn Val Ile Pro Ala
100 105 110

Leu Glu Leu Val Glu Pro Ile Lys Lys Asp Thr Val Gln Ala Lys Thr
115 120 125

Ser Val Ser Cys Gly Asp Met Arg Val Thr Trp Leu Lys Glu Val Ala
130 135 140

Lys Leu His Trp Thr Thr Thr Gly Leu Arg Lys Lys
145 150 155

<210> 645
<211> 115
<212> PRT
<213> Homo sapiens

<400> 645
Ala Asp Pro Gly Val Gly Ala Val Pro Gly Leu Ala Ala Asp Leu Ala
1 5 10 15

Thr Ala Ala Arg Ser Leu Gly Pro Ala Leu Val Leu Asp Leu Gly Arg
20 25 30

Pro Pro Ser Pro Asp Pro His Glu Gly Pro Ser Pro Ser Pro Arg Arg
35 40 45

Ser Pro Asp Leu Val Arg Gly Pro Gly Pro Gly Leu Gly Pro Gly Val
50 55 60

Leu Pro Gln Cys Pro Arg Gly Asn Pro Asn Pro Gly Arg Asp Arg Arg
65 70 75 80

Val Pro Pro Ser Leu Leu Lys Arg Lys Glu Arg Cys Pro Leu Lys Lys
85 90 95

Met Val Met Ser Gly Asn Pro Arg His Ile Thr Leu Ile His Lys Trp
100 105 110

Asp Leu Gly
115

<210> 646

<211> 153
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (127)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 646
Tyr Met Pro Asn Gly Ser Leu Asn Glu Leu Leu His Arg Lys Thr Glu
1 5 10 15

Tyr Pro Asp Val Ala Trp Pro Leu Arg Phe Arg Ile Leu His Glu Ile
20 25 30

Ala Leu Gly Val Asn Tyr Leu His Asn Met Thr Pro Pro Leu Leu His
35 40 45

His Asp Leu Lys Thr Gln Asn Ile Leu Leu Asp Asn Glu Phe His Val
50 55 60

Lys Ile Ala Asp Phe Gly Leu Ser Lys Trp Arg Met Met Ser Leu Ser
65 70 75 80

Gln Ser Arg Ser Ser Lys Ser Ala Pro Glu Gly Gly Thr Ile Ile Tyr
85 90 95

Met Pro Pro Glu Asn Tyr Glu Pro Gly Gln Lys Ser Arg Ala Ser Ile
100 105 110

Lys His Asp Ile Tyr Ser Tyr Ala Val Ile Thr Trp Glu Val Xaa Ser
115 120 125

Arg Lys Gln Pro Phe Glu Asp Val Thr Asn Pro Leu Gln Ile Met Tyr
130 135 140

Ser Val Ser Gln Gly His Trp Thr Gly
145 150

<210> 647
<211> 220
<212> PRT
<213> Homo sapiens

<400> 647
Ala Ser Glu Gln Gly Ala Val Gly Gln Gly Gly Leu Ala Gly Val Pro
1 5 10 15

Thr Leu Thr Ser Leu Pro Ser Ser Cys Pro Glu Pro Arg Pro Ser Met
20 25 30

Asp Ala Val Asp Ala Thr Met Glu Lys Leu Arg Ala Gln Cys Leu Ser
35 40 45

Arg Gly Ala Ser Gly Ile Gln Gly Leu Ala Arg Phe Phe Arg Gln Leu
50 55 60

Asp Arg Asp Gly Ser Arg Ser Leu Asp Ala Asp Glu Phe Arg Gln Gly
65 70 75 80

Leu Ala Lys Leu Gly Leu Val Leu Asp Gln Ala Glu Ala Glu Gly Val
85 90 95

Cys Arg Lys Trp Asp Arg Asn Gly Ser Gly Thr Leu Asp Leu Glu Glu
100 105 110

Phe Leu Arg Ala Leu Arg Pro Pro Met Ser Gln Ala Arg Glu Ala Val
115 120 125

Ile Ala Ala Ala Phe Ala Lys Leu Asp Arg Ser Gly Asp Gly Val Val
130 135 140

Thr Val Asp Asp Leu Arg Gly Val Tyr Ser Gly Arg Ala His Pro Lys
145 150 155 160

Val Arg Ser Gly Glu Trp Thr Glu Asp Glu Val Leu Arg Arg Phe Leu
165 170 175

Asp Asn Phe Asp Ser Ser Glu Lys Asp Gly Gln Val Thr Leu Ala Glu
180 185 190

Phe Gln Asp Tyr Tyr Ser Gly Val Ser Ala Ser Met Asn Thr Asp Glu
195 200 205

Glu Phe Val Ala Met Met Thr Ser Ala Trp Gln Leu
210 215 220

<210> 648
<211> 118
<212> PRT
<213> Homo sapiens

<400> 648
Asp Asn Arg Thr Leu Thr Lys Gly Pro Asp Thr Val Gly Thr Met Gly
1 5 10 15

Gln Cys Arg Ser Ala Asn Ala Glu Asp Ala Gln Glu Phe Ser Asp Val

```
            20                  25                  30

Glu Arg Ala Ile Glu Thr Leu Ile Lys Asn Phe His Gln Tyr Ser Val
        35                  40                  45

Glu Gly Gly Lys Glu Thr Leu Thr Pro Ser Glu Leu Arg Asp Leu Val
    50                  55                  60

Thr Gln Gln Leu Pro His Leu Met Pro Ser Asn Cys Gly Leu Glu Glu
65                  70                  75                  80

Lys Ile Ala Asn Leu Gly Ser Cys Asn Asp Ser Lys Leu Glu Phe Arg
                85                  90                  95

Ser Phe Trp Glu Leu Ile Gly Glu Ala Ala Lys Ser Val Lys Leu Glu
            100                 105                 110

Arg Pro Val Arg Gly His
        115



<210> 649
<211> 309
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (77)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (160)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 649
Asp His His Gln Gly Ala Glu Ser Val Pro Gly Ile Gly Val Ser Pro
 1               5                  10                  15

Thr Ser Ser Ser Ser Cys Pro Pro Thr Ser Cys Thr Gln Pro Val Thr
            20                  25                  30

Thr Trp Ser Pro Gly Leu Arg Val Glu Ser Leu Asp Gly Ala Lys Thr
        35                  40                  45

Gly Lys Gly Ala Leu Thr Gly Ala Pro Gly Ser Phe Gly Ser Ser Glu
    50                  55                  60

Phe Leu Thr Gly Leu Arg Asn Thr Ser Glu Ala Arg Xaa Thr Arg Gly
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65                  70                  75                  80

Pro Ile Met Gln Glu Pro Arg Arg Val Thr Pro Cys Leu Gly Lys Arg
                85                  90                  95

Gly Val Lys Thr Pro Gln Leu Gln Pro Gly Ser Ala Phe Leu Pro Arg
            100                 105                 110

Val Arg Arg Gln Ser Phe Pro Ala Arg Ser Asp Ser Tyr Thr Thr Val
        115                 120                 125

Arg Asp Phe Leu Ala Val Pro Arg Thr Ile Ser Ser Ala Ser Ala Thr
    130                 135                 140

Leu Ile Met Ala Val Ala Val Ser His Phe Arg Pro Gly Pro Glu Xaa
145                 150                 155                 160

Trp Asp Thr Ala Ser Met Ala Ala Ser Lys Val Lys Gln Asp Met Pro
                165                 170                 175

Pro Pro Gly Gly Tyr Gly Pro Ile Asp Tyr Lys Arg Asn Leu Pro Arg
            180                 185                 190

Arg Gly Leu Ser Gly Tyr Ser Met Leu Ala Ile Gly Ile Gly Thr Leu
        195                 200                 205

Ile Tyr Gly His Trp Ser Ile Met Lys Trp Asn Arg Glu Arg Arg Arg
    210                 215                 220

Leu Gln Ile Glu Asp Phe Glu Ala Arg Ile Ala Leu Leu Pro Leu Leu
225                 230                 235                 240

Gln Ala Glu Thr Asp Arg Arg Thr Leu Gln Met Leu Arg Glu Asn Leu
                245                 250                 255

Glu Glu Glu Ala Ile Ile Met Lys Asp Val Pro Asp Trp Lys Val Gly
            260                 265                 270

Glu Ser Val Phe His Thr Thr Arg Trp Val Pro Pro Leu Ile Gly Glu
        275                 280                 285

Leu Tyr Gly Leu Arg Thr Thr Glu Glu Ala Leu His Ala Ser His Gly
    290                 295                 300

Phe Met Trp Tyr Thr
305
```

<210> 650
<211> 286

<212> PRT
<213> Homo sapiens

<400> 650

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Ile Pro Thr Leu Ile Thr Ala Phe Val Leu Ala Thr Ser Gln Ala Gln
  1               5                  10                  15

Ala Gly Trp Leu Gln His Asp Tyr Gly His Leu Ser Val Tyr Arg Lys
             20                  25                  30

Pro Lys Trp Asn His Leu Val His Lys Phe Val Ile Gly His Leu Lys
         35                  40                  45

Gly Ala Ser Ala Asn Trp Trp Asn His Arg His Phe Gln His His Ala
     50                  55                  60

Lys Pro Asn Ile Phe His Lys Asp Pro Asp Val Asn Met Leu His Val
 65                  70                  75                  80

Phe Val Leu Gly Glu Trp Gln Pro Ile Glu Tyr Gly Lys Lys Lys Leu
                 85                  90                  95

Lys Tyr Leu Pro Tyr Asn His Gln His Glu Tyr Phe Phe Leu Ile Gly
            100                 105                 110

Pro Pro Leu Leu Ile Pro Met Tyr Phe Gln Tyr Gln Ile Ile Met Thr
        115                 120                 125

Met Ile Val His Lys Asn Trp Val Asp Leu Ala Trp Ala Val Ser Tyr
    130                 135                 140

Tyr Ile Arg Phe Phe Ile Thr Tyr Ile Pro Phe Tyr Gly Ile Leu Gly
145                 150                 155                 160

Ala Leu Leu Phe Leu Asn Phe Ile Arg Phe Leu Glu Ser His Trp Phe
                165                 170                 175

Val Trp Val Thr Gln Met Asn His Ile Val Met Glu Ile Asp Gln Glu
            180                 185                 190

Ala Tyr Arg Asp Trp Phe Ser Ser Gln Leu Thr Ala Thr Cys Asn Val
        195                 200                 205

Glu Gln Ser Phe Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln
    210                 215                 220

Ile Glu His His Leu Phe Pro Thr Met Pro Arg His Asn Leu His Lys
225                 230                 235                 240

Ile Ala Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Ile Glu Tyr
                245                 250                 255
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Gln Glu Lys Pro Leu Leu Arg Ala Leu Leu Asp Ile Ile Arg Ser Leu
260 265 270

Lys Lys Ser Gly Lys Leu Trp Leu Asp Ala Tyr Leu His Lys
275 280 285

<210> 651
<211> 184
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (57)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (71)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (106)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 651
Glu Arg Gly Pro Ile Pro Val Cys Pro His Lys Ala Ala Ser Ser Val
1 5 10 15

Ile Ser Leu Leu Arg Ala Glu Leu Arg Leu Tyr Thr Asp Pro His Lys
20 25 30

Tyr His Xaa Phe Cys Leu Arg Lys Asp Lys Ala His Val Cys Phe Cys
35 40 45

Phe Arg Phe Leu Phe Ser Phe Phe Xaa Glu Ala Leu Trp Arg Ser Met
50 55 60

Phe Leu Leu Ser Phe Leu Xaa Lys Pro Ser Phe Trp Ala Thr Gly Leu
65 70 75 80

Ile Leu Ser Thr Ser Ser Phe Pro Pro Phe Ser Ile Val Ser Leu Pro

85 90 95

Pro Ser His Pro Thr Arg Ala Pro Leu Xaa Leu Ser Phe Pro Ser Ser
100 105 110

Pro Ala Val Ser Phe Leu Arg Ser Gly Thr Lys Leu Ile Phe Arg Arg
115 120 125

Arg Pro Arg Gln Lys Glu Ala Gly Leu Ser Gln Ser His Asp Asp Leu
130 135 140

Ser Asn Ala Thr Ala Thr Pro Ser Val Arg Lys Lys Ala Gly Ser Phe
145 150 155 160

Ser Arg Arg Leu Ile Lys Arg Phe Ser Phe Lys Ser Lys Pro Lys Ala
165 170 175

Asn Gly Asn Pro Ser Pro Gln Leu
180

<210> 652
<211> 641
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (438)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 652
Gln Gly Ser Glu Pro Ser Ser Glu Asn Ala Asn Asp Thr Ile Ile Leu
1 5 10 15

Arg Asn Leu Asn Pro His Ser Thr Met Asp Ser Ile Leu Gly Ala Leu
20 25 30

Ala Pro Tyr Ala Val Leu Ser Ser Ser Asn Val Arg Val Ile Lys Asp
35 40 45

Lys Gln Thr Gln Leu Asn Arg Gly Phe Ala Phe Ile Gln Leu Ser Thr
50 55 60

Ile Glu Ala Ala Gln Leu Leu Gln Ile Leu Gln Ala Leu His Pro Pro
65 70 75 80

Leu Thr Ile Asp Gly Lys Thr Ile Asn Val Glu Phe Ala Lys Gly Ser
85 90 95

Lys Arg Asp Met Ala Ser Asn Glu Gly Ser Arg Ile Ser Ala Ala Ser
100 105 110

Val Ala Ser Thr Ala Ile Ala Ala Ala Gln Trp Ala Ile Ser Gln Ala
115 120 125

Ser Gln Gly Gly Glu Gly Thr Trp Ala Thr Ser Glu Glu Pro Pro Val
130 135 140

Asp Tyr Ser Tyr Tyr Gln Gln Asp Glu Gly Tyr Gly Asn Ser Gln Gly
145 150 155 160

Thr Glu Ser Ser Leu Tyr Ala His Gly Tyr Leu Lys Gly Thr Lys Gly
165 170 175

Pro Gly Ile Thr Gly Thr Lys Gly Asp Pro Thr Gly Ala Gly Pro Glu
180 185 190

Ala Ser Leu Glu Pro Gly Ala Asp Ser Val Ser Met Gln Ala Phe Ser
195 200 205

Arg Ala Gln Pro Gly Ala Ala Pro Gly Ile Tyr Gln Gln Ser Ala Glu
210 215 220

Ala Ser Ser Ser Gln Gly Thr Ala Ala Asn Ser Gln Ser Tyr Thr Ile
225 230 235 240

Met Ser Pro Ala Val Leu Lys Ser Glu Leu Gln Ser Pro Thr His Pro
245 250 255

Ser Ser Ala Leu Pro Pro Ala Thr Ser Pro Thr Ala Gln Glu Ser Tyr
260 265 270

Ser Gln Tyr Pro Val Pro Asp Val Ser Thr Tyr Gln Tyr Asp Glu Thr
275 280 285

Ser Gly Tyr Tyr Tyr Asp Pro Gln Thr Gly Leu Tyr Tyr Asp Pro Asn
290 295 300

Ser Gln Tyr Tyr Tyr Asn Ala Gln Ser Gln Gln Tyr Leu Tyr Trp Asp
305 310 315 320

Gly Glu Arg Arg Thr Tyr Val Pro Ala Leu Glu Gln Ser Ala Asp Gly
325 330 335

His Lys Glu Thr Gly Ala Pro Ser Lys Glu Gly Lys Glu Lys Lys Glu
340 345 350

Lys His Lys Thr Lys Thr Ala Gln Gln Ile Ala Lys Asp Met Glu Arg
355 360 365

Trp Ala Arg Ser Leu Asn Lys Gln Lys Glu Asn Phe Lys Asn Ser Phe
370 375 380

Gln Pro Ile Ser Ser Leu Arg Asp Asp Glu Arg Arg Glu Ser Ala Thr
385 390 395 400

Ala Asp Ala Gly Tyr Ala Ile Leu Glu Lys Lys Gly Ala Leu Ala Glu
405 410 415

Arg Gln His Thr Ser Met Asp Leu Pro Lys Leu Ala Ser Asp Asp Arg
420 425 430

Pro Ser Pro Pro Arg Xaa Leu Val Ala Ala Tyr Ser Gly Glu Ser Asp
435 440 445

Ser Glu Glu Glu Gln Glu Arg Gly Gly Pro Glu Arg Glu Glu Lys Leu
450 455 460

Thr Asp Trp Gln Lys Leu Ala Cys Leu Leu Cys Arg Arg Gln Phe Pro
465 470 475 480

Ser Lys Glu Ala Leu Ile Arg His Gln Gln Leu Ser Gly Leu His Lys
485 490 495

Gln Asn Leu Glu Ile His Arg Arg Ala His Leu Ser Glu Asn Glu Leu
500 505 510

Glu Ala Leu Glu Lys Asn Asp Met Glu Gln Met Lys Tyr Arg Asp Arg
515 520 525

Ala Ala Glu Arg Arg Glu Lys Tyr Gly Ile Pro Glu Pro Pro Glu Pro
530 535 540

Lys Arg Arg Lys Tyr Gly Gly Ile Ser Thr Ala Ser Val Asp Phe Glu
545 550 555 560

Gln Pro Thr Arg Asp Gly Leu Gly Ser Asp Asn Ile Gly Ser Arg Met
565 570 575

Leu Gln Ala Met Gly Trp Lys Glu Gly Ser Gly Leu Gly Arg Lys Lys
580 585 590

Gln Gly Ile Val Thr Pro Ile Glu Ala Gln Thr Arg Val Arg Gly Ser
595 600 605

Gly Leu Gly Ala Arg Gly Ser Ser Tyr Gly Val Thr Ser Thr Glu Ser
610 615 620

Tyr Lys Glu Thr Leu His Lys Thr Met Val Thr Arg Phe Asn Glu Ala
625 630 635 640

Gln

<210> 653
<211> 516
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (247)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 653
```
Xaa Thr Arg Pro Gly Arg Gln Thr Arg Leu Cys Arg Pro Ala Ile Ser
  1               5                  10                  15

Leu Leu Trp Leu Val Thr Pro Gly Val Pro Ala Phe Ser Gly Trp Gly
             20                  25                  30

Arg Arg His Arg Gly Arg Thr Gly Arg Arg Ala Met Ala Ser Cys Val
         35                  40                  45

Gly Ser Arg Thr Leu Ser Lys Asp Asp Val Asn Tyr Lys Met His Phe
     50                  55                  60

Arg Met Ile Asn Glu Gln Gln Val Glu Asp Ile Thr Ile Asp Phe Phe
 65                  70                  75                  80

Tyr Arg Pro His Thr Ile Thr Leu Leu Ser Phe Thr Ile Val Ser Leu
                 85                  90                  95

Met Tyr Phe Ala Phe Thr Arg Asp Asp Ser Val Pro Glu Asp Asn Ile
            100                 105                 110

Trp Arg Gly Ile Leu Ser Val Ile Phe Phe Phe Leu Ile Ile Ser Val
        115                 120                 125

Leu Ala Phe Pro Asn Gly Pro Phe Thr Arg Pro His Pro Ala Leu Trp
    130                 135                 140

Arg Met Val Phe Gly Leu Ser Val Leu Tyr Phe Leu Phe Leu Val Phe
145                 150                 155                 160
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Leu Leu Phe Leu Asn Phe Glu Gln Val Lys Ser Leu Met Tyr Trp Leu
                165                 170                 175

Asp Pro Asn Leu Arg Tyr Ala Thr Arg Glu Ala Asp Val Met Glu Tyr
            180                 185                 190

Ala Val Asn Cys His Val Ile Thr Trp Glu Arg Ile Ile Ser His Phe
        195                 200                 205

Asp Ile Phe Ala Phe Gly His Phe Trp Gly Trp Ala Met Lys Ala Leu
    210                 215                 220

Leu Ile Arg Ser Tyr Gly Leu Cys Trp Thr Ile Ser Ile Thr Trp Glu
225                 230                 235                 240

Leu Thr Glu Leu Phe Phe Xaa His Leu Leu Pro Asn Phe Ala Glu Cys
                245                 250                 255

Trp Trp Asp Gln Val Ile Leu Asp Ile Leu Leu Cys Asn Gly Gly Gly
            260                 265                 270

Ile Trp Leu Gly Met Val Val Cys Arg Phe Leu Glu Met Arg Thr Tyr
        275                 280                 285

His Trp Ala Ser Phe Lys Asp Ile His Thr Thr Thr Gly Lys Ile Lys
    290                 295                 300

Arg Ala Val Leu Gln Phe Thr Pro Ala Ser Trp Thr Tyr Val Arg Trp
305                 310                 315                 320

Phe Asp Pro Lys Ser Ser Phe Gln Arg Val Ala Gly Val Tyr Leu Phe
                325                 330                 335

Met Ile Ile Trp Gln Leu Thr Glu Leu Asn Thr Phe Phe Leu Lys His
            340                 345                 350

Ile Phe Val Phe Gln Ala Ser His Pro Leu Ser Trp Gly Arg Ile Leu
        355                 360                 365

Phe Ile Gly Gly Ile Thr Ala Pro Thr Val Arg Gln Tyr Tyr Ala Tyr
    370                 375                 380

Leu Thr Asp Thr Gln Cys Lys Arg Val Gly Thr Gln Cys Trp Val Phe
385                 390                 395                 400

Gly Val Ile Gly Phe Leu Glu Ala Ile Val Cys Ile Lys Phe Gly Gln
                405                 410                 415

Asp Leu Phe Ser Lys Thr Gln Ile Leu Tyr Val Val Leu Trp Leu Leu
            420                 425                 430
```

Cys Val Ala Phe Thr Thr Phe Leu Cys Leu Tyr Gly Met Ile Trp Tyr
435 440 445

Ala Glu His Tyr Gly His Arg Glu Lys Thr Tyr Ser Glu Cys Glu Asp
450 455 460

Gly Thr Tyr Ser Pro Glu Ile Ser Trp His His Arg Lys Gly Thr Lys
465 470 475 480

Gly Ser Glu Asp Ser Pro Pro Lys His Ala Gly Asn Asn Glu Ser His
485 490 495

Ser Ser Arg Arg Arg Asn Arg His Ser Lys Ser Lys Val Thr Asn Gly
500 505 510

Val Gly Lys Lys
515

<210> 654
<211> 663
<212> PRT
<213> Homo sapiens

<400> 654
Leu Glu Cys Arg Glu Ala His Ile Arg Asp Val Pro Val Val Arg Leu
1 5 10 15

Pro Ala Asp Ser Pro Ile Pro Glu Arg Gly Asp Leu Ser Cys Arg Met
20 25 30

His Thr Cys Phe Asp Val Tyr Arg Cys Gly Phe Asn Pro Lys Asn Lys
35 40 45

Ile Lys Val Tyr Ile Tyr Ala Leu Lys Lys Tyr Val Asp Asp Phe Gly
50 55 60

Val Ser Val Ser Asn Thr Ile Ser Arg Glu Tyr Asn Glu Leu Leu Met
65 70 75 80

Ala Ile Ser Asp Ser Asp Tyr Tyr Thr Asp Asp Ile Asn Arg Ala Cys
85 90 95

Leu Phe Val Pro Ser Ile Asp Val Leu Asn Gln Asn Thr Leu Arg Ile
100 105 110

Lys Glu Thr Ala Gln Ala Met Ala Gln Leu Ser Arg Trp Asp Arg Gly
115 120 125

Thr Asn His Leu Leu Phe Asn Met Leu Pro Gly Gly Pro Pro Asp Tyr

```
    130                 135                 140

Asn Thr Ala Leu Asp Val Pro Arg Asp Arg Ala Leu Leu Ala Gly Gly
145                 150                 155                 160

Gly Phe Ser Thr Trp Thr Tyr Arg Gln Gly Tyr Asp Val Ser Ile Pro
                165                 170                 175

Val Tyr Ser Pro Leu Ser Ala Glu Val Asp Leu Pro Glu Lys Gly Pro
            180                 185                 190

Gly Pro Arg Gln Tyr Phe Leu Leu Ser Ser Gln Val Gly Leu His Pro
        195                 200                 205

Glu Tyr Arg Glu Asp Leu Glu Ala Leu Gln Val Lys His Gly Glu Ser
    210                 215                 220

Val Leu Val Leu Asp Lys Cys Thr Asn Leu Ser Glu Gly Val Leu Ser
225                 230                 235                 240

Val Arg Lys Arg Cys His Lys His Gln Val Phe Asp Tyr Pro Gln Val
                245                 250                 255

Leu Gln Glu Ala Thr Phe Cys Val Val Leu Arg Gly Ala Arg Leu Gly
            260                 265                 270

Gln Ala Val Leu Ser Asp Val Leu Gln Ala Gly Cys Val Pro Val Val
        275                 280                 285

Ile Ala Asp Ser Tyr Ile Leu Pro Phe Ser Glu Val Leu Asp Trp Lys
    290                 295                 300

Arg Ala Ser Val Val Val Pro Glu Glu Lys Met Ser Asp Val Tyr Ser
305                 310                 315                 320

Ile Leu Gln Ser Ile Pro Gln Arg Gln Ile Glu Glu Met Gln Arg Gln
                325                 330                 335

Ala Arg Trp Phe Trp Glu Ala Tyr Phe Gln Ser Ile Lys Ala Ile Ala
            340                 345                 350

Leu Ala Thr Leu Gln Ile Ile Asn Asp Arg Ile Tyr Pro Tyr Ala Ala
        355                 360                 365

Ile Ser Tyr Glu Glu Trp Asn Asp Pro Pro Ala Val Lys Trp Gly Ser
    370                 375                 380

Val Ser Asn Pro Leu Phe Leu Pro Leu Ile Pro Pro Gln Ser Gln Gly
385                 390                 395                 400

Phe Thr Ala Ile Val Leu Thr Tyr Asp Arg Val Glu Ser Leu Phe Arg
```

```
            405                 410                 415

Val Ile Thr Glu Val Ser Lys Val Pro Ser Leu Ser Lys Leu Leu Val
            420                 425                 430

Val Trp Asn Asn Gln Asn Lys Asn Pro Pro Glu Asp Ser Leu Trp Pro
        435                 440                 445

Lys Ile Arg Val Pro Leu Lys Val Val Arg Thr Ala Glu Asn Lys Leu
    450                 455                 460

Ser Asn Arg Phe Phe Pro Tyr Asp Glu Ile Glu Thr Glu Ala Val Leu
465                 470                 475                 480

Ala Ile Asp Asp Asp Ile Ile Met Leu Thr Ser Asp Glu Leu Gln Phe
                485                 490                 495

Gly Tyr Glu Val Trp Arg Glu Phe Pro Asp Arg Leu Val Gly Tyr Pro
            500                 505                 510

Gly Arg Leu His Leu Trp Asp His Glu Met Asn Lys Trp Lys Tyr Glu
        515                 520                 525

Ser Glu Trp Thr Asn Glu Val Ser Met Val Leu Thr Gly Ala Ala Phe
    530                 535                 540

Tyr His Lys Tyr Phe Asn Tyr Leu Tyr Thr Tyr Lys Met Pro Gly Asp
545                 550                 555                 560

Ile Lys Asn Trp Val Asp Ala His Met Asn Cys Glu Asp Ile Ala Met
                565                 570                 575

Asn Phe Leu Val Ala Asn Val Thr Gly Lys Ala Val Ile Lys Val Thr
            580                 585                 590

Pro Arg Lys Lys Phe Lys Cys Pro Glu Cys Thr Ala Ile Asp Gly Leu
        595                 600                 605

Ser Leu Asp Gln Thr His Met Val Glu Arg Ser Glu Cys Ile Asn Lys
    610                 615                 620

Phe Ala Ser Val Phe Gly Thr Met Pro Leu Lys Val Val Glu His Arg
625                 630                 635                 640

Ala Asp Pro Val Leu Tyr Lys Asp Asp Phe Pro Glu Lys Leu Lys Ser
                645                 650                 655

Phe Pro Asn Ile Gly Ser Leu
            660
```

<210> 655
<211> 97
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (91)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 655
Ala Thr Gln Leu Leu Ser Ser Phe Ser Val Gly Pro Leu Leu Gln Ile
1 5 10 15

Thr Phe Tyr Glu Asp Lys Asn Phe Gln Gly Arg Arg Tyr Asp Cys Asp
20 25 30

Cys Asp Cys Ala Asp Xaa His Thr Tyr Leu Ser Arg Cys Asn Ser Ile
35 40 45

Lys Val Glu Gly Gly Thr Trp Ala Val Tyr Glu Arg Pro Asn Phe Ala
50 55 60

Gly Tyr Met Tyr Ile Leu Pro Gln Gly Glu Tyr Pro Glu Tyr Gln Arg
65 70 75 80

Trp Met Gly Leu Asn Asp Arg Leu Ser Ser Xaa Arg Ala Val Ser Ser
85 90 95

Ala

<210> 656
<211> 167
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (73)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 656
```
Asp Ala Asp Leu Val Ile Trp Asp Pro Asp Ser Val Lys Thr Ile Ser
  1               5                  10                  15

Ala Lys Thr His Asn Ser Ser Leu Glu Tyr Asn Ile Phe Glu Gly Met
             20                  25                  30

Glu Cys Arg Gly Ser Pro Leu Val Val Ile Ser Gln Gly Lys Ile Val
         35                  40                  45

Leu Glu Asp Gly Thr Leu His Val Thr Glu Xaa Ser Gly Arg Tyr Ile
     50                  55                  60

Pro Arg Lys Pro Phe Pro Asp Phe Xaa Tyr Lys Arg Ile Lys Ala Arg
 65                  70                  75                  80

Ser Arg Leu Ala Glu Leu Arg Gly Val Pro Arg Gly Leu Tyr Asp Gly
                 85                  90                  95

Pro Val Cys Glu Val Ser Val Thr Pro Lys Thr Val Thr Pro Ala Ser
            100                 105                 110

Ser Ala Lys Thr Ser Pro Ala Lys Gln Gln Ala Pro Pro Val Arg Asn
        115                 120                 125

Leu His Gln Ser Gly Phe Ser Leu Ser Gly Ala Gln Ile Asp Asp Asn
    130                 135                 140

Ile Pro Arg Arg Thr Thr Gln Arg Ile Val Ala Pro Pro Gly Gly Arg
145                 150                 155                 160

Ala Asn Ile Thr Ser Leu Gly
                165
```

<210> 657
<211> 176
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (26)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 657
```
Xaa Ser Leu Asn Leu Xaa Lys Leu Ala Leu His Arg Gly Gly Gly Arg
  1               5                  10                  15

Ser Arg Thr Ser Gly Ser Pro Gly Leu Xaa Glu Phe Gly Thr Ser Ala
             20                  25                  30

Val Leu Leu Arg Leu Gly Asp Glu Leu Glu Met Ile Arg Pro Ser Val
         35                  40                  45

Tyr Arg Asn Val Ala Arg Gln Leu His Ile Ser Leu Gln Ser Glu Pro
     50                  55                  60

Val Val Thr Asp Ala Phe Leu Ala Val Ala Gly His Ile Phe Ser Ala
 65                  70                  75                  80

Gly Ile Thr Trp Gly Lys Val Val Ser Leu Tyr Ala Val Ala Ala Gly
                 85                  90                  95

Leu Ala Val Asp Cys Val Arg Gln Ala Gln Pro Ala Met Val His Ala
            100                 105                 110

Leu Val Asp Cys Leu Gly Glu Phe Val Arg Lys Thr Leu Ala Thr Trp
        115                 120                 125

Leu Arg Arg Arg Gly Gly Trp Thr Asp Val Leu Lys Cys Val Val Ser
    130                 135                 140

Thr Asp Pro Gly Leu Arg Ser His Trp Leu Val Ala Ala Leu Cys Ser
145                 150                 155                 160

Phe Gly Arg Phe Leu Lys Ala Ala Phe Phe Val Leu Leu Pro Glu Arg
                165                 170                 175
```

<210> 658
<211> 137
<212> PRT

<213> Homo sapiens

<220>
<221> SITE
<222> (75)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (91)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (101)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (129)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (131)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 658
Gly Pro Val Gly Ser Ser Ser Glu Ala Pro Arg Gly Ala Gly Asp Ala
1 5 10 15

Gly Met Ala Gly Glu Leu Thr Pro Glu Glu Glu Ala Gln Tyr Lys Lys
20 25 30

Ala Phe Ser Ala Val Asp Thr Asp Gly Asn Gly Thr Ile Asn Ala Gln
35 40 45

Glu Leu Gly Ala Ala Leu Lys Ala Thr Gly Lys Asn Leu Ser Glu Ala
50 55 60

Gln Leu Arg Lys Leu Ile Ser Glu Val Asp Xaa Asp Gly Asp Gly Glu
65 70 75 80

Ile Ser Phe Gln Glu Phe Leu Thr Ala Ala Xaa Lys Ala Arg Ala Gly
85 90 95

Leu Glu Asp Leu Xaa Val Ala Phe Arg Ala Phe Asp Gln Asp Gly Asp
100 105 110

Gly His Ile Thr Val Asp Glu Leu Arg Arg Ala Xaa Ala Gly Leu Gly
115 120 125

Xaa Leu Xaa Glu Ile Asp His Phe Gly
130 135

<210> 659
<211> 34
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (28)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 659
Pro Xaa Ser Arg Gln Asp Val Met Asp Ile Val Phe Ile Glu Gln Leu
1 5 10 15

Ser Val Ile Thr Thr Ile Gly Val Tyr Asp Trp Xaa Gln Xaa Ser Asn
20 25 30

Arg Ser

<210> 660
<211> 56
<212> PRT
<213> Homo sapiens

<400> 660
Asn Pro Ile Ser Pro Lys Asn Tyr Lys Lys Ile Ser Gln Ala Gln Ser
1 5 10 15

Gln Leu Pro Val Ile Pro Ala Thr Gln Glu Ala Glu Ser Gly Glu Ser
20 25 30

Leu Gly Pro Gly Ala Ala Glu Val Asn Ser Glu Pro Arg Leu His His
35 40 45

Arg Thr Pro Ala Trp Ile Thr Lys
50 55

<210> 661
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (29)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (36)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (39)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 661
Tyr Ile Gly Phe Val Ile Leu Val Phe Phe Ala Ser Ser Tyr Val Lys
1 5 10 15

Glu Ile Asp Asn Lys Ile Leu Asn Asn Lys Lys Lys Xaa Lys Xaa Ser
20 25 30

Ser Lys Gly Xaa Val Ala Xaa Ala Ile
35 40

<210> 662
<211> 524

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (191)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 662

```
Cys Glu Ala Trp Arg Gly Arg Ala Asp Pro Gly Gly Gln Ser Cys Leu
  1               5                  10                  15

Gln Ala Leu Gln Asn Ser Thr Ala Pro Gln His Pro Gly Leu His Arg
             20                  25                  30

Trp Thr Gly Asp Arg Lys Met Pro Pro Arg Arg Asp Arg Gly Cys Asp
         35                  40                  45

Pro Val Gly Asn Ile Pro Gln Gly Glu Ser Gly Gly Trp Trp Pro Glu
     50                  55                  60

Gly Ala Gly Asp Leu Leu Gly Ala Thr Pro Asp Arg Glu Ser Pro Gln
 65                  70                  75                  80

Leu Pro Gly Gln Arg Leu Gln Pro His Pro Gln Gln Cys Leu His Gly
                 85                  90                  95

Arg Arg Val Arg Gly Pro Ser Trp Arg Val Glu Ala Trp Gly Pro Gly
            100                 105                 110

Leu His Val Phe Gly Pro Gly Gln Arg Trp Gly Xaa Ser Pro Gln Gly
        115                 120                 125

Ile Pro Glu Leu Glu Gln Tyr Asp Pro Pro Glu Leu Ala Asp Ser Ser
    130                 135                 140

Gly Arg Val Val Arg Glu Lys Trp Ser Ala Asp Met Trp Arg Leu Gly
145                 150                 155                 160

Cys Leu Ile Trp Glu Val Phe Asn Gly Pro Leu Pro Arg Ala Ala Ala
                165                 170                 175

Leu Arg Asn Pro Gly Lys Ile Pro Lys Thr Leu Val Pro His Xaa Cys
            180                 185                 190

Lys Leu Val Gly Ala Asn Pro Lys Val Arg Pro Asn Pro Ala Arg Phe
```

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        195                 200                 205

Leu Gln Asn Cys Arg Ala Pro Gly Gly Phe Met Ser Asn Arg Phe Val
    210                 215                 220

Glu Thr Asn Leu Phe Leu Glu Glu Ile Gln Ile Lys Glu Pro Ala Glu
225                 230                 235                 240

Lys Gln Lys Phe Phe Gln Glu Leu Ser Lys Ser Leu Asp Ala Phe Pro
                245                 250                 255

Glu Asp Phe Cys Arg His Lys Val Leu Pro Gln Leu Leu Thr Ala Phe
            260                 265                 270

Glu Phe Gly Asn Ala Gly Ala Val Val Leu Thr Pro Leu Phe Lys Val
        275                 280                 285

Gly Lys Phe Leu Ser Ala Glu Glu Tyr Gln Gln Lys Ile Ile Pro Val
    290                 295                 300

Val Val Lys Met Phe Ser Ser Thr Asp Arg Ala Met Arg Ile Arg Leu
305                 310                 315                 320

Leu Gln Gln Met Glu Gln Phe Ile Gln Tyr Leu Asp Glu Pro Thr Val
                325                 330                 335

Asn Thr Gln Ile Phe Pro His Val Val His Gly Phe Leu Asp Thr Asn
            340                 345                 350

Pro Ala Ile Arg Glu Gln Thr Val Lys Ser Met Leu Leu Leu Ala Pro
        355                 360                 365

Lys Leu Asn Glu Ala Asn Leu Asn Val Glu Leu Met Lys His Phe Ala
    370                 375                 380

Arg Leu Gln Ala Lys Asp Glu Gln Gly Pro Ile Arg Cys Asn Thr Thr
385                 390                 395                 400

Val Cys Leu Gly Lys Ile Gly Ser Tyr Leu Ser Ala Ser Thr Arg His
                405                 410                 415

Arg Val Leu Thr Ser Ala Phe Ser Arg Ala Thr Arg Asp Pro Phe Ala
            420                 425                 430

Pro Ser Arg Val Ala Gly Val Leu Gly Phe Ala Ala Thr His Asn Leu
        435                 440                 445

Tyr Ser Met Asn Asp Cys Ala Gln Lys Ile Leu Pro Val Leu Cys Gly
    450                 455                 460

Leu Thr Val Asp Pro Glu Lys Ser Val Arg Asp Gln Ala Phe Lys Ala
```

465 470 475 480

Phe Gly Ala Ser Cys Pro Asn Trp Ser Leu Cys Arg Arg Thr Arg Pro
485 490 495

Ser Trp Arg Lys Trp Arg Arg Met Ser Met Gln Pro Pro Ala Leu Ala
500 505 510

Trp Glu Glu Pro Gln Leu Ala Gly Gln Ala Gly Pro
515 520

<210> 663
<211> 272
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (29)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 663
Pro Thr Leu Asp Ser Ala Arg Ser Leu Ser Met Arg Ala Pro Ser Leu
1 5 10 15

Thr Pro Ser Ala Ala Pro Leu Ser Thr Trp Pro Leu Xaa Ile Leu Val
20 25 30

Arg Ser Gly His Asn Arg Ala Val Asp Trp Trp Ser Leu Gly Ala Leu
35 40 45

Met Tyr Asp Met Leu Thr Gly Ser Pro Pro Phe Thr Ala Glu Asn Arg
50 55 60

Lys Lys Thr Met Asp Lys Ile Ile Arg Gly Lys Leu Ala Leu Pro Pro
65 70 75 80

Tyr Leu Thr Pro Asp Ala Arg Asp Leu Val Lys Lys Phe Leu Lys Arg
85 90 95

Asn Pro Ser Gln Arg Ile Gly Gly Gly Pro Gly Asp Ala Ala Asp Val
100 105 110

Gln Arg His Pro Phe Phe Arg His Met Asn Trp Asp Asp Leu Leu Ala
115 120 125

Trp Arg Val Asp Pro Pro Phe Arg Pro Cys Leu Gln Ser Glu Glu Asp
130 135 140

Val Ser Gln Phe Asp Thr Arg Phe Thr Arg Gln Thr Pro Val Asp Ser
145 150 155 160

Pro Asp Asp Thr Ala Leu Ser Glu Ser Ala Asn Gln Ala Phe Leu Gly
165 170 175

Phe Thr Tyr Val Ala Pro Ser Val Leu Asp Ser Ile Lys Glu Gly Phe
180 185 190

Ser Phe Gln Pro Lys Leu Arg Ser Pro Arg Arg Leu Asn Ser Ser Pro
195 200 205

Arg Ala Pro Val Ser Pro Leu Lys Phe Ser Pro Phe Glu Gly Phe Arg
210 215 220

Pro Ser Pro Ser Leu Pro Glu Pro Thr Glu Leu Pro Leu Pro Pro Leu
225 230 235 240

Leu Pro Pro Pro Pro Pro Ser Thr Thr Ala Pro Leu Pro Ile Arg Pro
245 250 255

Pro Ser Gly Thr Lys Lys Ser Lys Arg Gly Arg Gly Arg Pro Gly Arg
260 265 270

<210> 664
<211> 256
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (99)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 664
Gly Thr Arg Arg Glu Thr Trp Arg Pro Gly Ser Met Ala Gly Leu Glu
1 5 10 15

Leu Leu Ser Asp Gln Gly Tyr Arg Val Asp Gly Arg Arg Ala Gly Glu
20 25 30

Leu Arg Lys Ile Gln Ala Arg Met Gly Val Phe Ala Gln Ala Asp Gly
35 40 45

Ser Ala Tyr Ile Glu Gln Gly Asn Thr Lys Ala Leu Ala Val Val Tyr
50 55 60

Gly Pro His Glu Ile Arg Gly Ser Arg Ala Arg Ala Leu Pro Asp Arg
65 70 75 80

Ala Leu Val Asn Cys Gln Tyr Ser Ser Ala Thr Phe Ser Thr Gly Glu
85 90 95

Arg Lys Xaa Arg Pro His Gly Asp Arg Lys Ser Cys Glu Met Gly Leu
100 105 110

Gln Leu Arg Gln Thr Phe Glu Ala Ala Ile Leu Thr Gln Leu His Pro
115 120 125

Arg Ser Gln Ile Asp Ile Tyr Val Gln Val Leu Gln Ala Asp Gly Gly
130 135 140

Thr Tyr Ala Ala Cys Val Asn Ala Ala Thr Leu Ala Val Leu Asp Ala
145 150 155 160

Gly Ile Pro Met Arg Asp Phe Val Cys Ala Cys Ser Ala Gly Phe Val
165 170 175

Asp Gly Thr Ala Leu Ala Asp Leu Ser His Val Glu Glu Ala Ala Gly
180 185 190

Gly Pro Gln Leu Ala Leu Ala Leu Leu Pro Ala Ser Gly Gln Ile Ala
195 200 205

Leu Leu Glu Met Asp Ala Arg Leu His Glu Asp His Leu Glu Arg Val
210 215 220

Leu Glu Ala Ala Ala Gln Ala Ala Arg Asp Val His Thr Leu Leu Asp
225 230 235 240

Arg Val Val Arg Gln His Val Arg Glu Ala Ser Ile Leu Leu Gly Asp
245 250 255

<210> 665
<211> 241
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (122)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 665
Pro Arg Gly Asp Lys Ala Arg Thr Xaa Pro Pro Ala Ala Ser Ala Arg
1   5   10   15

Pro Ser Arg Ser Lys Arg Gly Gly Glu Glu Arg Val Leu Glu Lys Glu
            20   25   30

Glu Glu Glu Asp Asp Asp Glu Asp Glu Asp Glu Glu Asp Asp Val Ser
        35   40   45

Glu Gly Ser Glu Val Pro Glu Ser Asp Arg Pro Ala Gly Ala Gln His
    50   55   60

His Gln Leu Asn Gly Glu Arg Gly Pro Gln Ser Ala Lys Glu Arg Val
65   70   75   80

Lys Glu Trp Thr Pro Cys Gly Pro His Gln Gly Gln Asp Glu Gly Arg
                85   90   95

Gly Pro Ala Pro Gly Ser Gly Thr Arg Gln Val Phe Ser Met Ala Ala
            100   105   110

Met Asn Lys Glu Gly Gly Thr Ala Ser Xaa Ala Thr Gly Pro Asp Ser
        115   120   125

Pro Ser Pro Val Pro Leu Pro Pro Gly Lys Pro Ala Leu Pro Gly Ala
    130   135   140

Asp Gly Thr Pro Phe Gly Cys Pro Pro Gly Arg Lys Glu Lys Pro Ser
145   150   155   160

Asp Pro Val Glu Trp Thr Val Met Asp Val Val Glu Tyr Phe Thr Glu
                165   170   175

Ala Gly Phe Pro Glu Gln Ala Thr Val Phe Gln Glu Gln Glu Ile Asp
            180   185   190

Gly Lys Ser Leu Leu Leu Met Gln Arg Thr Asp Val Leu Thr Gly Leu
        195   200   205

Ser Ile Arg Leu Gly Pro Ala Leu Lys Ile Tyr Glu His His Ile Lys
    210   215   220

Val Leu Gln Gln Gly His Phe Glu Asp Asp Asp Pro Asp Gly Phe Leu
225   230   235   240

Gly

<210> 666
<211> 131
<212> PRT
<213> Homo sapiens

<400> 666
Val Thr Gly Gly Gly Ala Val Val Leu Gly Ala Glu Ser His Ala Ser
1   5   10   15

Lys Asp Val Ala Ile Asp Met Met Asp Ser Arg Thr Ser Gln Gln Leu
            20   25   30

Gln Leu Ile Asp Glu Gln Asp Ser Tyr Ile Gln Ser Arg Ala Asp Thr
        35   40   45

Met Gln Asn Ile Glu Ser Thr Ile Val Glu Leu Gly Ser Ile Phe Gln
    50   55   60

Gln Leu Ala His Met Val Lys Glu Gln Glu Glu Thr Ile Gln Arg Ile
65   70   75   80

Asp Glu Asn Val Leu Gly Ala Gln Leu Asp Val Glu Ala Ala His Ser
                85   90   95

Glu Ile Leu Lys Tyr Phe Gln Ser Val Thr Ser Asn Arg Trp Leu Met
            100   105   110

Val Lys Ile Phe Leu Ile Leu Ile Val Phe Phe Ile Ile Phe Val Val
        115   120   125

Phe Leu Ala
    130

<210> 667
<211> 652
<212> PRT
<213> Homo sapiens

<400> 667
Leu Ser Trp Asn Arg Tyr Thr Ser Val Ser Pro Leu His Arg Ser Leu
1   5   10   15

Gln Leu Pro Pro Arg Val Ser Gly Val Arg Cys Asp Gln Cys Ala Arg

20 25 30

Gly Phe Ser Gly Ile Phe Pro Ala Cys His Pro Cys His Ala Cys Phe
35 40 45

Gly Asp Trp Asp Arg Val Val Gln Asp Leu Ala Ala Arg Thr Gln Arg
50 55 60

Leu Glu Gln Arg Ala Gln Glu Leu Gln Gln Thr Gly Val Leu Gly Ala
65 70 75 80

Phe Glu Ser Ser Phe Trp His Met Gln Glu Lys Leu Gly Ile Val Gln
85 90 95

Gly Ile Val Gly Ala Arg Asn Thr Ser Ala Ala Ser Thr Ala Gln Leu
100 105 110

Val Glu Ala Thr Glu Glu Leu Arg Arg Glu Ile Gly Glu Ala Thr Glu
115 120 125

His Leu Thr Gln Leu Glu Ala Asp Leu Thr Asp Val Gln Asp Glu Asn
130 135 140

Phe Asn Ala Asn His Ala Leu Ser Gly Leu Glu Arg Asp Arg Leu Ala
145 150 155 160

Leu Asn Leu Thr Leu Arg Gln Leu Asp Gln His Leu Asp Leu Leu Lys
165 170 175

His Ser Asn Phe Leu Gly Ala Tyr Asp Ser Ile Arg His Ala His Ser
180 185 190

Gln Ser Ala Glu Ala Glu Arg Arg Ala Asn Thr Ser Ala Leu Ala Val
195 200 205

Pro Ser Pro Val Ser Asn Ser Ala Ser Ala Arg His Arg Thr Glu Ala
210 215 220

Leu Met Asp Ala Gln Lys Glu Asp Phe Asn Ser Lys His Met Ala Asn
225 230 235 240

Gln Arg Ala Leu Gly Lys Leu Ser Ala His Thr His Thr Leu Ser Leu
245 250 255

Thr Asp Ile Asn Glu Leu Val Cys Gly Ala Pro Gly Asp Ala Pro Cys
260 265 270

Ala Thr Ser Pro Cys Gly Gly Ala Gly Cys Arg Asp Glu Asp Gly Gln
275 280 285

Pro Arg Cys Gly Gly Leu Ser Cys Asn Gly Ala Ala Ala Thr Ala Asp

290 295 300

Leu Ala Leu Gly Arg Ala Arg His Thr Gln Ala Glu Leu Gln Arg Ala
305 310 315 320

Leu Ala Glu Gly Gly Ser Ile Leu Ser Arg Val Ala Glu Thr Arg Arg
325 330 335

Gln Ala Ser Glu Ala Gln Gln Arg Ala Gln Ala Ala Leu Asp Lys Ala
340 345 350

Asn Ala Ser Arg Gly Gln Val Glu Gln Ala Asn Gln Glu Leu Gln Glu
355 360 365

Leu Ile Gln Ser Val Lys Asp Phe Leu Asn Gln Glu Gly Ala Asp Pro
370 375 380

Asp Ser Ile Glu Met Val Ala Thr Arg Val Leu Glu Leu Ser Ile Pro
385 390 395 400

Ala Ser Ala Glu Gln Ile Gln His Leu Ala Gly Ala Ile Ala Glu Arg
405 410 415

Val Arg Ser Leu Ala Asp Val Asp Ala Ile Leu Ala Arg Thr Val Gly
420 425 430

Asp Val Arg Arg Ala Glu Gln Leu Leu Gln Asp Ala Arg Arg Ala Arg
435 440 445

Ser Trp Ala Glu Asp Glu Lys Gln Lys Ala Glu Thr Val Gln Ala Ala
450 455 460

Leu Glu Glu Ala Gln Arg Ala Gln Gly Ile Ala Gln Gly Ala Ile Arg
465 470 475 480

Gly Ala Val Ala Asp Thr Arg Asp Thr Glu Gln Thr Leu Tyr Gln Val
485 490 495

Gln Glu Arg Met Ala Gly Ala Glu Arg Ala Leu Ser Ser Ala Gly Glu
500 505 510

Arg Ala Arg Gln Leu Asp Ala Leu Leu Glu Ala Leu Lys Leu Lys Arg
515 520 525

Ala Gly Asn Ser Leu Ala Ala Ser Thr Ala Glu Glu Thr Ala Gly Ser
530 535 540

Ala Gln Gly Arg Ala Gln Glu Ala Glu Gln Leu Leu Arg Gly Pro Leu
545 550 555 560

Gly Asp Gln Tyr Gln Thr Val Lys Ala Leu Ala Glu Arg Lys Ala Gln

565 570 575

Gly Val Leu Ala Ala Gln Ala Arg Ala Glu Gln Leu Arg Asp Glu Ala
580 585 590

Arg Asp Leu Leu Gln Ala Ala Gln Asp Lys Leu Gln Arg Leu Gln Glu
595 600 605

Leu Glu Gly Thr Tyr Glu Glu Asn Glu Arg Ala Leu Glu Ser Lys Ala
610 615 620

Ala Gln Leu Asp Gly Leu Glu Ala Arg Met Arg Ser Val Leu Gln Ala
625 630 635 640

Ile Asn Leu Gln Val Gln Ile Tyr Asn Thr Cys Gln
645 650

<210> 668
<211> 406
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 668
Gly Ala Val Arg Ser Ser Cys Ala Glu Leu Gln Ala Arg Val Met Ala
1 5 10 15

Ala Leu Arg Gln Pro Gln Val Ala Glu Cys Trp Pro Arg Pro Gly Glu
20 25 30

Pro Ser Gly Arg Ser Ser Gly Pro Ser Pro Ser Trp Pro Cys Gln Arg
35 40 45

Arg Ala Ala Cys Asn Leu Ile Gly Glu His Thr Asp Tyr Asn Gln Gly
50 55 60

Leu Val Leu Pro Met Ala Leu Glu Leu Met Thr Val Leu Val Gly Ser
65 70 75 80

Pro Arg Lys Xaa Gly Leu Val Ser Leu Leu Thr Thr Ser Glu Gly Ala
85 90 95

Asp Glu Pro Gln Arg Leu Gln Phe Pro Leu Pro Thr Ala Gln Arg Ser
100 105 110

Leu Glu Pro Gly Thr Pro Arg Trp Ala Asn Tyr Val Lys Gly Val Ile
115 120 125

Gln Tyr Tyr Pro Ala Ala Pro Leu Pro Gly Phe Ser Ala Val Val Val
130 135 140

Ser Ser Val Pro Leu Gly Gly Gly Leu Ser Ser Ser Ala Ser Leu Glu
145 150 155 160

Val Ala Thr Tyr Thr Phe Leu Gln Gln Leu Cys Pro Asp Ser Gly Thr
165 170 175

Ile Ala Ala Arg Ala Gln Val Cys Gln Gln Ala Glu His Ser Phe Ala
180 185 190

Gly Met Pro Cys Gly Ile Met Asp Gln Phe Ile Ser Leu Met Gly Gln
195 200 205

Lys Gly His Ala Leu Leu Ile Asp Cys Arg Ser Leu Glu Thr Ser Leu
210 215 220

Val Pro Leu Ser Asp Pro Lys Leu Ala Val Leu Ile Thr Asn Ser Asn
225 230 235 240

Val Arg His Ser Leu Ala Ser Ser Glu Tyr Pro Val Arg Arg Arg Gln
245 250 255

Cys Glu Glu Val Ala Arg Ala Leu Gly Lys Glu Ser Leu Arg Glu Val
260 265 270

Gln Leu Glu Glu Leu Glu Ala Ala Arg Asp Leu Val Ser Lys Glu Gly
275 280 285

Phe Arg Arg Ala Arg His Val Val Gly Glu Ile Arg Arg Thr Ala Gln
290 295 300

Ala Ala Ala Ala Leu Arg Arg Gly Asp Tyr Arg Ala Phe Gly Arg Leu
305 310 315 320

Met Val Glu Ser His Arg Ser Leu Arg Asp Asp Tyr Glu Val Ser Cys
325 330 335

Pro Glu Leu Asp Gln Leu Val Glu Ala Ala Leu Ala Val Pro Gly Val
340 345 350

Tyr Gly Ser Arg Met Thr Gly Gly Gly Phe Gly Gly Cys Thr Val Thr
355 360 365

Leu Leu Glu Ala Ser Ala Ala Pro His Ala Met Arg His Ile Gln Glu
370 375 380

His Tyr Gly Gly Thr Ala Thr Phe Tyr Leu Ser Gln Ala Ala Asp Gly
385 390 395 400

Ala Lys Val Leu Cys Leu
405

<210> 669
<211> 86
<212> PRT
<213> Homo sapiens

<400> 669
Pro Glu Pro Thr Val Val Met Ala Ala Arg Ala Leu Cys Met Leu Gly
1 5 10 15

Leu Val Leu Ala Leu Leu Ser Ser Ser Ser Ala Glu Glu Tyr Val Gly
20 25 30

Leu Ser Ala Asn Gln Cys Ala Val Pro Ala Lys Asp Arg Val Asp Cys
35 40 45

Gly Tyr Pro His Val Thr Pro Lys Glu Cys Asn Asn Arg Gly Cys Cys
50 55 60

Phe Asp Ser Arg Ile Pro Gly Val Pro Trp Cys Phe Lys Pro Leu Gln
65 70 75 80

Glu Ala Glu Cys Thr Phe
85

<210> 670
<211> 392
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 670
Gly Gly Gly Ala Arg Xaa Ser Pro Ala Thr Gln Pro Pro Pro Leu Leu
1 5 10 15

Pro Pro Ser Ala Thr Gly Pro Asp Ala Thr Val Gly Gly Pro Ala Pro
20 25 30

```
Thr Pro Leu Leu Pro Pro Ser Ala Thr Ala Ser Val Lys Met Glu Pro
        35                  40                  45

Glu Asn Lys Tyr Leu Pro Glu Leu Met Ala Glu Lys Asp Ser Leu Asp
    50                  55                  60

Pro Ser Phe Thr His Ala Met Gln Leu Leu Thr Ala Glu Ile Glu Lys
65                  70                  75                  80

Ile Gln Lys Gly Asp Ser Lys Lys Asp Asp Glu Glu Asn Tyr Leu Asp
                85                  90                  95

Leu Phe Ser His Lys Asn Met Lys Leu Lys Glu Arg Val Leu Ile Pro
            100                 105                 110

Val Lys Gln Tyr Pro Lys Phe Asn Phe Val Gly Lys Ile Leu Gly Pro
        115                 120                 125

Gln Gly Asn Thr Ile Lys Arg Leu Gln Glu Glu Thr Gly Ala Lys Ile
    130                 135                 140

Ser Val Leu Gly Lys Gly Ser Met Arg Asp Lys Ala Lys Glu Glu Glu
145                 150                 155                 160

Leu Arg Lys Gly Gly Asp Pro Lys Tyr Ala His Leu Asn Met Asp Leu
                165                 170                 175

His Val Phe Ile Glu Val Phe Gly Pro Pro Cys Glu Ala Tyr Ala Leu
            180                 185                 190

Met Ala His Ala Met Glu Glu Val Lys Lys Phe Leu Val Pro Asp Met
        195                 200                 205

Met Asp Asp Ile Cys Gln Glu Gln Phe Leu Glu Leu Ser Tyr Leu Asn
    210                 215                 220

Gly Val Pro Glu Pro Ser Arg Gly Arg Gly Val Pro Val Arg Gly Arg
225                 230                 235                 240

Gly Ala Ala Pro Pro Pro Pro Pro Val Pro Arg Gly Arg Gly Val Gly
                245                 250                 255

Pro Pro Arg Gly Ala Leu Val Arg Gly Thr Pro Val Arg Gly Ala Ile
            260                 265                 270

Thr Arg Gly Ala Thr Val Thr Arg Gly Val Pro Pro Pro Pro Thr Val
        275                 280                 285

Arg Gly Ala Pro Ala Pro Arg Ala Arg Thr Ala Gly Ile Gln Arg Ile
    290                 295                 300
```

Pro Leu Pro Pro Pro Pro Ala Pro Glu Thr Tyr Glu Glu Tyr Gly Tyr
305 310 315 320

Asp Asp Thr Tyr Ala Glu Gln Ser Tyr Glu Gly Tyr Glu Gly Tyr Tyr
325 330 335

Ser Gln Ser Gln Gly Asp Ser Glu Tyr Tyr Asp Tyr Gly His Gly Glu
340 345 350

Val Gln Asp Ser Tyr Glu Ala Tyr Gly Gln Asp Asp Trp Asn Gly Thr
355 360 365

Arg Pro Ser Leu Lys Ala Pro Pro Ala Arg Pro Val Lys Gly Ala Tyr
370 375 380

Arg Glu His Pro Tyr Gly Arg Tyr
385 390

<210> 671
<211> 180
<212> PRT
<213> Homo sapiens

<400> 671
Arg Asn Met Ser Ser Phe Ser Arg Ala Pro Gln Gln Trp Ala Thr Phe
1 5 10 15

Ala Arg Ile Trp Tyr Leu Leu Asp Gly Lys Met Gln Pro Pro Gly Lys
20 25 30

Leu Ala Ala Met Ala Ser Ile Arg Leu Gln Gly Leu His Lys Pro Val
35 40 45

Tyr His Ala Leu Ser Asp Cys Gly Asp His Val Val Ile Met Asn Thr
50 55 60

Arg His Ile Ala Phe Ser Gly Asn Lys Trp Glu Gln Lys Val Tyr Ser
65 70 75 80

Ser His Thr Gly Tyr Pro Gly Gly Phe Arg Gln Val Thr Ala Ala Gln
85 90 95

Leu His Leu Arg Asp Pro Val Ala Ile Val Lys Leu Ala Ile Tyr Gly
100 105 110

Met Leu Pro Lys Asn Leu His Arg Arg Thr Met Met Glu Arg Leu His
115 120 125

Leu Phe Pro Asp Glu Tyr Ile Pro Glu Asp Ile Leu Lys Asn Leu Val

130 135 140

Glu Glu Leu Pro Gln Pro Arg Lys Ile Pro Lys Arg Leu Asp Glu Tyr
145 150 155 160

Thr Gln Glu Glu Ile Asp Ala Phe Pro Arg Leu Trp Thr Pro Pro Glu
165 170 175

Asp Tyr Arg Leu
180

<210> 672
<211> 78
<212> PRT
<213> Homo sapiens

<400> 672
Glu Asn Tyr Gln Phe Thr Tyr Arg Arg Phe Phe Phe Pro Asn Ser Arg
1 5 10 15

Phe His Pro Arg Pro Phe Glu Glu Leu Gln Thr Leu Ser Leu Arg Lys
20 25 30

Glu Arg Gly Gln Pro Lys Ile Asn Ala Lys Phe Ala Tyr Thr Pro Ser
35 40 45

His Ser Asp Val Leu Val Val Thr Tyr Tyr Gln Cys Gly Arg Glu Pro
50 55 60

Lys Leu His Phe Arg Ser Lys Tyr Ser Leu Cys Arg Tyr Cys
65 70 75

<210> 673
<211> 139
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (113)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (132)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 673
Pro Thr Arg Pro Pro Leu Cys Arg Gly Ala Ala Ser Arg Gly Leu Leu
1   5   10   15

Cys Lys Trp Ala Pro Trp Pro Ser Ala Pro Val Pro Ala Thr Arg Asp
            20   25   30

Arg Ala Pro Arg Pro Ala Arg Gly Arg Arg Pro Gly Arg Leu Gly Ser
        35   40   45

Thr Ser Ser Asn Ser Ser Cys Ser Ser Thr Glu Cys Pro Gly Glu Ala
    50   55   60

Ile Pro His Pro Pro Gly Leu Pro Lys Ala Asp Pro Gly His Trp Trp
65   70   75   80

Ala Ser Phe Phe Phe Gly Lys Ser Thr Leu Pro Phe Met Ala Thr Val
                85   90   95

Leu Glu Ser Ala Glu His Ser Glu Pro Pro Gln Ala Ser Ser Ser Met
            100   105   110

Xaa Ala Cys Gly Leu Ala Arg Glu Ala Pro Arg Lys Gln Pro Gly Gly
        115   120   125

Gln Ser Ser Xaa Ala Ser Ala Gly Pro Pro Ser
    130   135

<210> 674
<211> 279
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (58)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (193)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 674

Glu Arg Ala His Ser Leu Xaa His Gly Val Asp Gly Glu Pro Cys Pro
1 5 10 15

Glu Asp Tyr Lys Tyr Ile Ser Glu Asn Cys Glu Thr Ser Thr Met Asn
20 25 30

Ile Asp Arg Asn Ile Thr His Leu Gln His Cys Thr Phe Val Asp Asp
35 40 45

Cys Ser Ser Ser Asn Cys Leu Cys Gly Xaa Phe Ser Ile Arg Cys Trp
50 55 60

Tyr Asp Lys Asp Gly Arg Leu Leu Gln Glu Phe Asn Lys Ile Glu Pro
65 70 75 80

Pro Leu Ile Phe Glu Cys Asn Gln Ala Cys Ser Cys Trp Arg Asn Cys
85 90 95

Lys Asn Arg Val Val Gln Ser Gly Ile Lys Val Arg Leu Gln Leu Tyr
100 105 110

Arg Thr Ala Lys Met Gly Trp Gly Val Arg Ala Leu Gln Thr Ile Pro
115 120 125

Gln Gly Thr Phe Ile Cys Glu Tyr Val Gly Glu Leu Ile Ser Asp Ala
130 135 140

Glu Ala Asp Val Arg Glu Asp Asp Ser Tyr Leu Phe Asp Leu Asp Asn
145 150 155 160

Lys Asp Gly Glu Val Tyr Cys Ile Asp Ala Arg Tyr Tyr Gly Asn Ile
165 170 175

Ser Arg Phe Ile Asn His Leu Cys Asp Pro Asn Ile Ile Pro Val Arg
180 185 190

Xaa Phe Met Leu His Gln Asp Leu Arg Phe Pro Arg Ile Ala Phe Phe
195 200 205

Ser Ser Arg Asp Ile Arg Thr Gly Glu Glu Leu Gly Phe Asp Tyr Gly
210 215 220

Asp Arg Phe Trp Asp Ile Lys Ser Lys Tyr Phe Thr Cys Gln Cys Gly
225 230 235 240

Ser Glu Lys Cys Lys His Ser Ala Glu Ala Ile Ala Leu Glu Gln Ser
245 250 255

Arg Leu Ala Arg Leu Asp Pro His Pro Glu Leu Leu Pro Glu Leu Gly
260 265 270

Ser Leu Pro Pro Val Asn Thr
275

<210> 675
<211> 405
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (393)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (394)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 675
Arg Asn Thr Leu Gly Arg Gly Thr Thr Ile Thr Leu Val Leu Lys Glu
1 5 10 15

Glu Ala Ser Asp Tyr Leu Glu Leu Asp Thr Ile Lys Asn Leu Val Lys
20 25 30

Lys Tyr Ser Gln Phe Ile Asn Phe Pro Ile Tyr Val Trp Ser Ser Lys
35 40 45

Thr Glu Thr Val Glu Glu Pro Met Glu Glu Glu Glu Ala Ala Lys Glu
50 55 60

Glu Lys Glu Glu Ser Asp Asp Glu Ala Ala Val Glu Glu Glu Glu Glu
65 70 75 80

Glu Lys Lys Pro Lys Thr Lys Lys Val Glu Lys Thr Val Trp Asp Trp
85 90 95

Glu Leu Met Asn Asp Ile Lys Pro Ile Trp Gln Arg Pro Ser Lys Glu
100 105 110

Val Glu Glu Asp Glu Tyr Lys Ala Phe Tyr Lys Ser Phe Ser Lys Glu
115 120 125

Ser Asp Asp Pro Met Ala Tyr Ile His Phe Thr Ala Glu Gly Glu Val
130 135 140

Thr Phe Lys Ser Ile Leu Phe Val Pro Thr Ser Ala Pro Arg Gly Leu
145 150 155 160

```
Phe Asp Glu Tyr Gly Ser Lys Lys Ser Asp Tyr Ile Lys Leu Tyr Val
                165                 170                 175

Arg Arg Val Phe Ile Thr Asp Asp Phe His Asp Met Met Pro Lys Tyr
            180                 185                 190

Leu Asn Phe Val Lys Gly Val Val Asp Ser Asp Asp Leu Pro Leu Asn
        195                 200                 205

Val Ser Arg Glu Thr Leu Gln Gln His Lys Leu Leu Lys Val Ile Arg
    210                 215                 220

Lys Lys Leu Val Arg Lys Thr Leu Asp Met Ile Lys Lys Ile Ala Asp
225                 230                 235                 240

Asp Lys Tyr Asn Asp Thr Phe Trp Lys Glu Phe Gly Thr Asn Ile Lys
                245                 250                 255

Leu Gly Val Ile Glu Asp His Ser Asn Arg Thr Arg Leu Ala Lys Leu
            260                 265                 270

Leu Arg Phe Gln Ser Ser His His Pro Thr Asp Ile Thr Ser Leu Asp
        275                 280                 285

Gln Tyr Val Glu Arg Met Lys Glu Lys Gln Asp Lys Ile Tyr Phe Met
    290                 295                 300

Ala Gly Ser Ser Arg Lys Glu Ala Glu Ser Ser Pro Phe Val Glu Arg
305                 310                 315                 320

Leu Leu Lys Lys Gly Tyr Glu Val Ile Tyr Leu Thr Glu Pro Val Asp
                325                 330                 335

Glu Tyr Cys Ile Gln Ala Leu Pro Glu Phe Asp Gly Lys Arg Phe Gln
            340                 345                 350

Asn Val Ala Lys Glu Gly Val Lys Phe Asp Glu Ser Glu Lys Thr Lys
        355                 360                 365

Glu Ser Arg Glu Ala Val Glu Lys Glu Phe Glu Pro Leu Leu Asn Trp
    370                 375                 380

Met Lys Asp Lys Ala Leu Lys Gly Xaa Xaa Leu Trp Glu Ile Leu Pro
385                 390                 395                 400

Ile Cys Gly Lys Tyr
                405
```

<210> 676

<211> 465
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 676
```
Asn Asp Ser Leu Xaa Xaa Lys Ala Gly Thr Pro Ala Gly Asn Arg Xaa
  1               5                  10                  15

Gly Ile Pro Gly Ser Thr His Ala Ser Ala Ala Ala Pro Phe Ala Ala
             20                  25                  30

Ala Leu Ala Arg Asp Pro Asn Pro Ala Ser Pro Leu Pro Glu His Arg
         35                  40                  45

Pro Arg Leu His Arg Gly Pro Gly Pro Pro Ala Arg Leu Ala Ala Ala
     50                  55                  60

Met Ala Asp Pro Lys Tyr Ala Asp Leu Pro Gly Ile Ala Arg Asn Glu
 65                  70                  75                  80

Pro Asp Val Tyr Glu Thr Ser Asp Leu Pro Glu Asp Asp Gln Ala Glu
                 85                  90                  95

Phe Asp Ala Glu Glu Leu Thr Ser Thr Ser Val Glu His Ile Ile Val
            100                 105                 110

Asn Pro Asn Ala Ala Tyr Asp Lys Phe Lys Asp Lys Arg Val Gly Thr
        115                 120                 125

Lys Gly Leu Asp Phe Ser Asp Arg Ile Gly Lys Thr Lys Arg Thr Gly
    130                 135                 140

Tyr Glu Ser Gly Glu Tyr Glu Met Leu Gly Glu Gly Leu Gly Val Lys
145                 150                 155                 160

Glu Thr Pro Gln Gln Lys Tyr Gln Arg Leu Leu His Glu Val Gln Glu
```

165 170 175

Leu Thr Thr Glu Val Glu Lys Ile Lys Thr Thr Val Lys Glu Ser Ala
180 185 190

Thr Glu Glu Lys Leu Thr Pro Val Leu Leu Ala Lys Gln Leu Ala Ala
195 200 205

Leu Lys Gln Gln Leu Val Ala Ser His Leu Glu Lys Leu Leu Gly Pro
210 215 220

Asp Ala Ala Ile Asn Leu Thr Asp Pro Asp Gly Ala Leu Ala Lys Arg
225 230 235 240

Leu Leu Leu Gln Leu Glu Ala Thr Lys Asn Ser Lys Gly Gly Ser Gly
245 250 255

Gly Lys Thr Thr Gly Thr Pro Pro Asp Ser Ser Leu Val Thr Tyr Glu
260 265 270

Leu His Ser Arg Pro Glu Gln Asp Lys Phe Ser Gln Ala Ala Lys Val
275 280 285

Ala Glu Leu Glu Lys Arg Leu Thr Glu Leu Glu Thr Ala Val Arg Cys
290 295 300

Asp Gln Asp Ala Gln Asn Pro Leu Ser Ala Gly Leu Gln Gly Ala Cys
305 310 315 320

Leu Met Glu Thr Val Glu Leu Leu Gln Ala Lys Val Ser Ala Leu Asp
325 330 335

Leu Ala Val Leu Asp Gln Val Glu Ala Arg Leu Gln Ser Val Leu Gly
340 345 350

Lys Val Asn Glu Ile Ala Lys His Lys Ala Ser Val Glu Asp Ala Asp
355 360 365

Thr Gln Ser Lys Val His Gln Leu Tyr Glu Thr Ile Gln Arg Trp Ser
370 375 380

Pro Ile Ala Ser Thr Leu Pro Glu Leu Val Gln Arg Leu Val Thr Ile
385 390 395 400

Lys Gln Leu His Glu Gln Ala Met Gln Phe Gly Gln Leu Leu Thr His
405 410 415

Leu Asp Thr Thr Gln Gln Met Ile Ala Asn Ser Leu Lys Asp Asn Thr
420 425 430

Thr Leu Leu Thr Gln Val Gln Thr Thr Met Arg Glu Asn Leu Ala Thr

435 440 445

Val Glu Gly Asn Phe Ala Ser Ile Asp Glu Arg Met Lys Lys Leu Gly
450 455 460

Lys
465

<210> 677
<211> 48
<212> PRT
<213> Homo sapiens

<400> 677
Ser Ser Phe Leu Asn Ser Asp Leu Gly Leu Ser Leu Ala Arg Asn Leu
1 5 10 15

Ala Phe Ser Phe Thr Thr Lys Glu Arg Asp Gln Lys Pro Leu Ile Phe
20 25 30

Asn Phe His Lys Met Leu Glu Val Tyr Ile Tyr Ile Tyr Ile Phe Leu
35 40 45

<210> 678
<211> 940
<212> PRT
<213> Homo sapiens

<400> 678
Val Leu Gly Glu Gly Ile Ser Phe Leu Leu Ser Pro Pro Leu Pro Thr
1 5 10 15

Pro Ser Ile Asn Ile Ile Leu Leu Lys Ile Leu Arg Cys Gln Ala Ala
20 25 30

Lys Val Glu Ser Ala Ile Ala Glu Gly Gly Ala Ser Arg Phe Ser Ala
35 40 45

Ser Ser Gly Gly Gly Gly Ser Arg Gly Ala Pro Gln His Tyr Pro Lys
50 55 60

Thr Ala Gly Asn Ser Glu Phe Leu Gly Lys Thr Pro Gly Gln Asn Ala
65 70 75 80

Gln Lys Trp Ile Pro Ala Arg Ser Thr Arg Arg Asp Asp Asn Ser Ala
85 90 95

Ala Asn Asn Ser Ala Asn Glu Lys Glu Arg His Asp Ala Ile Phe Arg
100 105 110

Lys Val Arg Gly Ile Leu Asn Lys Leu Thr Pro Glu Lys Phe Asp Lys
115 120 125

Leu Cys Leu Glu Leu Leu Asn Val Gly Val Glu Ser Lys Leu Ile Leu
130 135 140

Lys Gly Val Ile Leu Leu Ile Val Asp Lys Ala Leu Glu Glu Pro Lys
145 150 155 160

Tyr Ser Ser Leu Tyr Ala Gln Leu Cys Leu Arg Leu Ala Glu Asp Ala
165 170 175

Pro Asn Phe Asp Gly Pro Ala Ala Glu Gly Gln Pro Gly Gln Lys Gln
180 185 190

Ser Thr Thr Phe Arg Arg Leu Leu Ile Ser Lys Leu Gln Asp Glu Phe
195 200 205

Glu Asn Arg Thr Arg Asn Val Asp Val Tyr Asp Lys Arg Glu Asn Pro
210 215 220

Leu Leu Pro Glu Glu Glu Glu Gln Arg Ala Ile Ala Lys Ile Lys Met
225 230 235 240

Leu Gly Asn Ile Lys Phe Ile Gly Glu Leu Gly Lys Leu Asp Leu Ile
245 250 255

His Glu Ser Ile Leu His Lys Cys Ile Lys Thr Leu Leu Glu Lys Lys
260 265 270

Lys Arg Val Gln Leu Lys Asp Met Gly Glu Asp Leu Glu Cys Leu Cys
275 280 285

Gln Ile Met Arg Thr Val Gly Pro Arg Leu Asp His Glu Arg Ala Lys
290 295 300

Ser Leu Met Asp Gln Tyr Phe Ala Arg Met Cys Ser Leu Met Leu Ser
305 310 315 320

Lys Glu Leu Pro Ala Arg Ile Arg Phe Leu Leu Gln Asp Thr Val Glu
325 330 335

Leu Arg Glu His His Trp Val Pro Arg Lys Ala Phe Leu Asp Asn Gly
340 345 350

```
Pro Lys Thr Ile Asn Gln Ile Arg Gln Asp Ala Val Lys Asp Leu Gly
        355                 360                 365

Val Phe Ile Pro Ala Pro Met Ala Gln Gly Met Arg Ser Asp Phe Phe
    370                 375                 380

Leu Glu Gly Pro Phe Met Pro Pro Arg Met Lys Met Asp Arg Asp Pro
385                 390                 395                 400

Leu Gly Gly Leu Ala Asp Met Phe Gly Gln Met Pro Gly Ser Gly Ile
                405                 410                 415

Gly Thr Gly Pro Gly Val Ile Gln Asp Arg Phe Ser Pro Thr Met Gly
            420                 425                 430

Arg His Arg Ser Asn Gln Leu Phe Asn Gly His Gly Gly His Ile Met
        435                 440                 445

Pro Pro Thr Gln Ser Gln Phe Gly Glu Met Gly Gly Lys Phe Met Lys
    450                 455                 460

Ser Gln Gly Leu Ser Gln Leu Tyr His Asn Gln Ser Gln Gly Leu Leu
465                 470                 475                 480

Ser Gln Leu Gln Gly Gln Ser Lys Asp Met Pro Pro Arg Phe Ser Lys
                485                 490                 495

Lys Gly Gln Leu Asn Ala Asp Glu Ile Ser Leu Arg Pro Ala Gln Ser
            500                 505                 510

Phe Leu Met Asn Lys Asn Gln Val Pro Lys Leu Gln Pro Gln Ile Thr
        515                 520                 525

Met Ile Pro Pro Ser Ala Gln Pro Pro Arg Thr Gln Thr Pro Pro Leu
    530                 535                 540

Gly Gln Thr Pro Gln Leu Gly Leu Lys Thr Asn Pro Pro Leu Ile Gln
545                 550                 555                 560

Glu Lys Pro Ala Lys Thr Ser Lys Lys Pro Pro Pro Ser Lys Glu Glu
                565                 570                 575

Leu Leu Lys Leu Thr Glu Thr Val Val Thr Glu Tyr Leu Asn Ser Gly
            580                 585                 590

Asn Ala Asn Glu Ala Val Asn Gly Val Arg Glu Met Arg Ala Pro Lys
        595                 600                 605

His Phe Leu Pro Glu Met Leu Ser Lys Val Ile Ile Leu Ser Leu Asp
    610                 615                 620
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Arg Ser Asp Glu Asp Lys Glu Lys Ala Ser Ser Leu Ile Ser Leu Leu
625                 630                 635                 640

Lys Gln Glu Gly Ile Ala Thr Ser Asp Asn Phe Met Gln Ala Phe Leu
                645                 650                 655

Asn Val Leu Asp Gln Cys Pro Lys Leu Glu Val Asp Ile Pro Leu Val
            660                 665                 670

Lys Ser Tyr Leu Ala Gln Phe Ala Ala Arg Ala Ile Ile Ser Glu Leu
        675                 680                 685

Val Ser Ile Ser Glu Leu Ala Gln Pro Leu Glu Ser Gly Thr His Phe
    690                 695                 700

Pro Leu Phe Leu Leu Cys Leu Gln Gln Leu Ala Lys Leu Gln Asp Arg
705                 710                 715                 720

Glu Trp Leu Thr Glu Leu Phe Gln Gln Ser Lys Val Asn Met Gln Lys
                725                 730                 735

Met Leu Pro Glu Ile Asp Gln Asn Lys Asp Arg Met Leu Glu Ile Leu
            740                 745                 750

Glu Gly Lys Gly Leu Ser Phe Leu Phe Pro Leu Leu Lys Leu Glu Lys
        755                 760                 765

Glu Leu Leu Lys Gln Ile Lys Leu Asp Pro Ser Pro Gln Thr Ile Tyr
    770                 775                 780

Lys Trp Ile Lys Asp Asn Ile Ser Pro Lys Leu His Val Asp Lys Gly
785                 790                 795                 800

Phe Val Asn Ile Leu Met Thr Ser Phe Leu Gln Tyr Ile Ser Ser Glu
                805                 810                 815

Val Asn Pro Pro Ser Asp Glu Thr Asp Ser Ser Ser Ala Pro Ser Lys
            820                 825                 830

Glu Gln Leu Glu Gln Glu Lys Gln Leu Leu Leu Ser Phe Lys Pro Val
        835                 840                 845

Met Gln Lys Phe Leu His Asp His Val Asp Leu Gln Val Ser Ala Leu
    850                 855                 860

Tyr Ala Leu Gln Val His Cys Tyr Asn Ser Asn Phe Pro Lys Gly Met
865                 870                 875                 880

Leu Leu Arg Phe Phe Val His Phe Tyr Asp Met Glu Ile Ile Glu Glu
                885                 890                 895
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Glu Ala Phe Leu Ala Trp Lys Glu Asp Ile Thr Gln Glu Phe Pro Gly
900 905 910

Lys Gly Lys Ala Leu Phe Gln Val Asn Gln Trp Leu Thr Trp Leu Glu
915 920 925

Thr Ala Glu Glu Glu Glu Ser Glu Glu Glu Ala Asp
930 935 940

<210> 679
<211> 212
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (160)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (172)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 679
Ser Trp Lys Glu Glu Glu Xaa Lys Pro His Leu Gln Gly Lys Pro Gly
1 5 10 15

Arg Pro Leu Ser Pro Ala Asn Val Pro Ala Leu Pro Gly Glu Thr Val
20 25 30

Thr Ser Pro Val Arg Leu His Pro Asp Tyr Leu Ser Pro Glu Glu Ile
35 40 45

Gln Arg Gln Leu Gln Asp Ile Glu Arg Arg Leu Asp Ala Leu Glu Leu
50 55 60

Arg Gly Val Glu Leu Glu Lys Arg Leu Arg Ala Ala Glu Gly Asp Asp
65 70 75 80

Ala Glu Asp Ser Leu Met Val Asp Trp Phe Trp Leu Ile His Glu Lys
85 90 95

Gln Leu Leu Leu Arg Gln Glu Ser Glu Leu Met Tyr Lys Ser Lys Ala

100 105 110

Gln Arg Leu Glu Glu Gln Gln Leu Asp Ile Glu Gly Glu Leu Arg Arg
115 120 125

Leu Met Ala Lys Pro Glu Ala Leu Lys Ser Leu Gln Glu Arg Arg Arg
130 135 140

Glu Gln Glu Leu Leu Glu Gln Tyr Val Ser Thr Val Asn Asp Arg Xaa
145 150 155 160

Asp Ile Val Asp Ser Leu Asp Glu Asp Arg Leu Xaa Glu Gln Glu Glu
165 170 175

Asp Gln Met Leu Arg Asp Met Ile Glu Lys Leu Gly Leu Gln Arg Lys
180 185 190

Lys Ser Lys Phe Arg Leu Ser Lys Ile Trp Ser Pro Lys Ser Lys Ser
195 200 205

Ser Pro Ser Gln
210

<210> 680
<211> 412
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (172)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (404)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 680
Val Ala Val Glu Leu Gly Ser Leu Arg Gly Gly Thr Met Ala Ser Glu
1 5 10 15

Lys Pro Leu Ala Ala Val Thr Cys Thr Ala Pro Val Asn Ile Ala Val
20 25 30

Ile Lys Tyr Trp Gly Lys Arg Asp Glu Glu Leu Val Leu Pro Ile Asn
35 40 45

Ser Ser Leu Ser Val Thr Leu His Gln Asp Gln Leu Lys Thr Thr Thr

50 55 60

Thr Ala Val Ile Ser Lys Asp Phe Thr Glu Asp Arg Ile Trp Leu Asn
65 70 75 80

Gly Arg Glu Glu Asp Val Gly Gln Pro Arg Leu Gln Ala Cys Leu Arg
85 90 95

Glu Ile Arg Cys Leu Ala Arg Lys Arg Arg Asn Ser Arg Asp Gly Asp
100 105 110

Pro Leu Pro Ser Ser Leu Ser Cys Lys Val His Val Ala Ser Val Asn
115 120 125

Asn Phe Pro Thr Ala Ala Gly Leu Ala Ser Ser Ala Ala Gly Tyr Ala
130 135 140

Cys Leu Ala Tyr Thr Leu Ala Arg Val Tyr Gly Val Glu Ser Asp Leu
145 150 155 160

Ser Glu Val Ala Arg Arg Gly Ser Gly Ser Ala Xaa Arg Ser Leu Tyr
165 170 175

Gly Gly Phe Val Glu Trp Gln Met Gly Glu Gln Ala Asp Gly Lys Asp
180 185 190

Ser Ile Ala Arg Gln Val Ala Pro Glu Ser His Trp Pro Glu Leu Arg
195 200 205

Val Leu Ile Leu Val Val Ser Ala Glu Lys Lys Leu Thr Gly Ser Thr
210 215 220

Val Gly Met Arg Ala Ser Val Glu Thr Ser Pro Leu Leu Arg Phe Arg
225 230 235 240

Ala Glu Ser Val Val Pro Ala Arg Met Ala Glu Met Ala Arg Cys Ile
245 250 255

Arg Glu Arg Asp Phe Pro Ser Phe Ala Gln Leu Thr Met Lys Asp Ser
260 265 270

Asn Gln Phe His Ala Thr Cys Leu Asp Thr Phe Pro Pro Ile Ser Tyr
275 280 285

Leu Asn Ala Ile Ser Trp Arg Ile Ile His Leu Val His Arg Phe Asn
290 295 300

Ala His His Gly Asp Thr Lys Val Ala Tyr Thr Phe Asp Ala Gly Pro
305 310 315 320

Asn Ala Val Ile Phe Thr Leu Asp Asp Thr Val Ala Glu Phe Val Ala

325 330 335

Ala Val Trp His Gly Phe Pro Pro Gly Ser Asn Gly Asp Thr Phe Leu
340 345 350

Lys Gly Leu Gln Val Arg Pro Ala Pro Leu Ser Ala Glu Leu Gln Ala
355 360 365

Ala Leu Ala Met Glu Pro Thr Pro Gly Gly Val Lys Tyr Ile Ile Val
370 375 380

Thr Gln Val Gly Pro Gly Pro Gln Ile Leu Asp Asp Pro Cys Ala His
385 390 395 400

Leu Leu Gly Xaa Asp Gly Leu Pro Lys Pro Ala Ala
405 410

<210> 681
<211> 61
<212> PRT
<213> Homo sapiens

<400> 681
Lys Lys Thr Arg His Leu Ser Lys Ile Leu Cys Gly Lys Met Thr Val
1 5 10 15

Asn Lys Met Arg Val Ser Gly Pro Phe Val Leu Leu Ser Phe Phe Asp
20 25 30

Tyr Lys Phe Leu Leu Thr His Thr Ile Met Ser Ala Asn Pro Leu Leu
35 40 45

Pro Arg Glu Arg Asn Cys Ala Pro Ser Val Leu Leu Pro
50 55 60

<210> 682
<211> 243
<212> PRT
<213> Homo sapiens

<400> 682
Ser Ala Pro Pro Pro Pro Arg Arg Lys Thr Ala Pro Pro Ala His Arg
1 5 10 15

Gln Arg Pro Pro Pro Gln Ser Pro Thr Ala Thr Gly Leu Gly Pro Ala
20 25 30

```
Ala Arg Ser Cys Leu Pro Gln Pro Pro Ser Arg Gly Pro Gln Pro Pro
        35                  40                  45

Pro Thr Leu Pro His Gly Pro Gly Ala Met Ser Glu Leu Glu Gln Leu
    50                  55                  60

Arg Gln Glu Ala Glu Gln Leu Arg Asn Gln Ile Arg Asp Ala Arg Lys
65                  70                  75                  80

Ala Cys Gly Asp Ser Thr Leu Thr Gln Ile Thr Ala Gly Leu Asp Pro
                85                  90                  95

Val Gly Arg Ile Gln Met Arg Thr Arg Arg Thr Leu Arg Gly His Leu
            100                 105                 110

Ala Lys Ile Tyr Ala Met His Trp Gly Thr Asp Ser Arg Leu Leu Val
        115                 120                 125

Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp Ser Tyr Thr Thr
    130                 135                 140

Asn Lys Val His Ala Ile Pro Leu Arg Ser Ser Trp Val Met Thr Cys
145                 150                 155                 160

Ala Tyr Ala Pro Ser Gly Asn Phe Val Ala Cys Gly Gly Leu Asp Asn
                165                 170                 175

Ile Cys Ser Ile Tyr Ser Leu Lys Thr Arg Glu Ala Thr Ser Gly Ser
            180                 185                 190

Ala Gly Ser Cys Leu Ala Thr Leu Gly Thr Cys Arg Val Ala Ala Ser
        195                 200                 205

Trp Met Thr Thr Lys Ser Ser Pro Ala Leu Gly Ile Pro Pro Val Pro
    210                 215                 220

Cys Gly Thr Leu Arg Gln Ala Ser Arg Gln Trp Val Leu Leu Asp Thr
225                 230                 235                 240

Val Gly Met
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<210> 683
<211> 146
<212> PRT
<213> Homo sapiens

<220>
<221> SITE

<222> (133)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 683
Asp Leu Glu Gly Asp Ala Gly Tyr Thr Gly Gly Leu Arg Gln Gly His
1 5 10 15

Ala Gly Gly Ala Gly Glu Leu Ala Arg Thr Leu Ala Leu Lys Pro Thr
20 25 30

Ser Leu Glu Leu Phe Arg Thr Lys Val Asn Ala Leu Thr Tyr Gly Glu
35 40 45

Val Leu Arg Leu Arg Gln Thr Glu Arg Leu His Gln Glu Gly Thr Leu
50 55 60

Ala Pro Pro Ile Leu Glu Leu Arg Glu Lys Leu Lys Pro Glu Leu Met
65 70 75 80

Gly Leu Ile Arg Gln Gln Arg Leu Leu Arg Leu Cys Glu Gly Thr Leu
85 90 95

Phe Arg Lys Ile Ser Ser Arg Arg Arg Gln Asp Lys Leu Trp Phe Cys
100 105 110

Cys Leu Ser Pro Asn His Lys Leu Leu Gln Tyr Gly Asp Met Glu Glu
115 120 125

Gly Ala Ser Ala Xaa Pro Trp Arg Val Cys Pro Ser Asn Ser Leu Trp
130 135 140

Pro Thr
145

<210> 684
<211> 300
<212> PRT
<213> Homo sapiens

<400> 684
Val Tyr Ser Cys Gly Phe Gln Val Gln Ser Trp Ser Pro Arg Trp Ile
1 5 10 15

Trp Val Thr Thr Lys Ser Lys Ile Gly Ala Pro Arg Ser Ser Phe Cys
20 25 30

Trp His Arg Leu Pro Ser Thr Ser Gln Leu His Leu Cys Pro Ala Glu
35 40 45

Gly Glu Ala Pro Ser Ala Gly Glu Ala Ala Pro Arg Ala Pro Thr Gly
50 55 60

Ser Glu Pro Lys Pro Gly Ala Leu Pro Trp Gly Pro Arg Ala Pro Asp
65 70 75 80

Ser Glu Gly Gly Gly Gly Ala Gly Ala Ala Asp Pro Ala Ala Asn Ala
85 90 95

Gly His Gly Ala Ser Ser Glu Ala Glu Cys Gly Cys Gln Arg Thr Leu
100 105 110

Arg Pro Met Pro Ser Thr Pro Gly Pro Gly Ala Ala Ala Val Arg Ala
115 120 125

Leu Gly Gln Leu Phe His Ile Ala Cys Phe Thr Cys His Gln Cys Ala
130 135 140

Gln Gln Leu Gln Gly Gln Gln Phe Tyr Ser Leu Glu Gly Ala Pro Tyr
145 150 155 160

Cys Glu Gly Cys Tyr Thr Asp Thr Leu Glu Lys Cys Asn Thr Cys Gly
165 170 175

Glu Pro Ile Thr Asp Arg Met Leu Arg Ala Thr Gly Lys Ala Tyr His
180 185 190

Pro His Cys Phe Thr Cys Val Val Cys Ala Arg Pro Leu Glu Gly Thr
195 200 205

Ser Phe Ile Val Asp Gln Ala Asn Arg Pro His Cys Val Pro Asp Tyr
210 215 220

His Lys Gln Tyr Ala Pro Arg Cys Ser Val Cys Ser Glu Pro Ile Met
225 230 235 240

Pro Glu Pro Gly Arg Asp Glu Thr Val Arg Val Val Ala Leu Asp Lys
245 250 255

Asn Phe His Met Lys Cys Tyr Lys Cys Glu Asp Cys Gly Lys Pro Leu
260 265 270

Ser Ile Glu Ala Asp Asp Asn Gly Cys Phe Pro Leu Asp Gly His Val
275 280 285

Leu Cys Arg Lys Cys His Thr Ala Arg Ala Gln Thr
290 295 300

<210> 685

<211> 130
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (61)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 685
Ile Arg His Glu Asp Cys Pro Thr Pro Ser Gln Cys Val Val Ala Arg
1 5 10 15

Thr Leu Gly Lys Gln Gln Thr Val Met Ala Ile Ala Thr Lys Ile Ala
20 25 30

Leu Gln Met Asn Cys Lys Met Gly Gly Glu Leu Trp Arg Val Asp Ile
35 40 45

Pro Leu Lys Leu Val Met Ile Val Gly Ile Asp Cys Xaa His Asp Met
50 55 60

Thr Ala Gly Arg Arg Ser Ile Ala Gly Phe Val Ala Ser Ile Asn Glu
65 70 75 80

Gly Met Thr Arg Trp Phe Ser Arg Cys Ile Phe Gln Asp Arg Gly Gln
85 90 95

Glu Leu Val Asp Gly Leu Lys Val Cys Leu Gln Ala Ala Leu Arg Ala
100 105 110

Trp Asn Ser Cys Asn Glu Tyr Met Pro Ser Arg Ile Ile Val Tyr Arg
115 120 125

Val Ala
130

<210> 686
<211> 207
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 686
Ile Tyr Gln Val Tyr Asn Ala Leu Gln Glu Lys Val Gln Ala Val Cys

```
1               5                   10                  15

Ala Asp Val Glu Lys Ser Glu Arg Val Val Glu Ser Cys Gln Ala Glu
            20                  25                  30

Val Asn Lys Leu Arg Arg Gln Ile Thr Gln Arg Lys Asn Glu Lys Glu
        35                  40                  45

Gln Glu Arg Arg Leu Gln Gln Ala Val Leu Ser Arg Gln Met Pro Ser
    50                  55                  60

Glu Ser Leu Asp Pro Ala Phe Ser Pro Arg Met Pro Ser Ser Gly Phe
65                  70                  75                  80

Ala Ala Glu Xaa Arg Ser Thr Leu Gly Asp Ala Glu Ala Ser Asp Pro
                85                  90                  95

Pro Pro Pro Tyr Ser Asp Phe His Pro Asn Asn Gln Glu Ser Thr Leu
            100                 105                 110

Ser His Ser Arg Met Glu Arg Ser Val Phe Met Pro Arg Pro Gln Ala
        115                 120                 125

Val Gly Ser Ser Asn Tyr Ala Ser Thr Ser Ala Gly Leu Lys Tyr Pro
    130                 135                 140

Gly Ser Gly Ala Asp Leu Pro Pro Pro Gln Arg Ala Ala Gly Asp Ser
145                 150                 155                 160

Gly Glu Asp Ser Asp Asp Ser Asp Tyr Glu Asn Leu Ile Asp Pro Thr
                165                 170                 175

Glu Pro Ser Asn Ser Glu Tyr Ser His Ser Lys Asp Ser Arg Pro Met
            180                 185                 190

Ala His Pro Asp Glu Asp Pro Arg Asn Thr Gln Thr Ser Gln Ile
        195                 200                 205


<210> 687
<211> 101
<212> PRT
<213> Homo sapiens

<400> 687
Ala Arg Ala Gly Glu Glu Gly Val Val Thr Arg Trp Arg His Arg Leu
1               5                   10                  15

Gly Gln Gly Ala Cys Pro Trp Asp Arg Ser Arg Pro Met Glu Pro Pro
            20                  25                  30
```

Gly Arg Ser Ser Arg Ser Thr Ala Ser His Thr Leu His Gln Tyr Cys
35 40 45

Cys Pro Thr Gln Val Leu Asp Ser Met Lys Leu Thr Pro Ser Gly Arg
50 55 60

Leu Ala Glu Ser Arg Glu Glu Glu Glu Glu Glu Glu Thr Glu Glu Glu
65 70 75 80

Glu Glu Glu Asp Ala His Gln Phe Cys Cys Pro Ala Ser Glu Cys Ser
85 90 95

Ser Pro Ser Ser Arg
100

<210> 688
<211> 62
<212> PRT
<213> Homo sapiens

<400> 688
Glu Arg Asn Ala Asp Pro Pro Asp Val Ser Leu Gly Lys Ala Val Asn
1 5 10 15

Gln Leu Ile Phe Ile Glu Asp Leu Leu Cys Pro Leu His Arg Val Ala
20 25 30

Ser Val Arg Glu Ser Trp Phe Phe Pro Arg Asn Thr Asp Phe Leu Ser
35 40 45

Gly Arg Leu His Val Phe Ile Tyr Phe His His Ser Arg Phe
50 55 60

<210> 689
<211> 549
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (7)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 689

```
Xaa Arg Trp Ala Cys Gly Xaa Leu Leu Leu Leu Val Arg Gly Gln Gly
  1               5                  10                  15

Gln Asp Ser Ala Ser Pro Ile Arg Thr Thr His Thr Gly Gln Val Leu
             20                  25                  30

Gly Ser Leu Val His Val Lys Gly Ala Asn Ala Gly Val Gln Thr Phe
         35                  40                  45

Leu Gly Ile Pro Phe Ala Lys Pro Pro Leu Gly Pro Leu Arg Phe Ala
     50                  55                  60

Pro Pro Glu Pro Pro Glu Ser Trp Ser Gly Val Arg Asp Gly Thr Thr
 65                  70                  75                  80

His Pro Ala Met Cys Leu Gln Asp Leu Thr Ala Val Glu Ser Glu Phe
                 85                  90                  95

Leu Ser Gln Phe Asn Met Thr Phe Pro Ser Asp Ser Met Ser Glu Asp
            100                 105                 110

Cys Leu Tyr Leu Ser Ile Tyr Thr Pro Ala His Ser His Glu Gly Ser
        115                 120                 125

Asn Leu Pro Val Met Val Trp Ile His Gly Gly Ala Leu Val Phe Gly
    130                 135                 140

Met Ala Ser Leu Tyr Asp Gly Ser Met Leu Ala Ala Leu Glu Asn Val
145                 150                 155                 160

Val Val Val Ile Ile Gln Tyr Arg Leu Gly Val Leu Gly Phe Phe Ser
                165                 170                 175

Thr Gly Asp Lys His Ala Thr Gly Asn Trp Gly Tyr Leu Asp Gln Val
            180                 185                 190

Ala Ala Leu Arg Trp Val Gln Gln Asn Ile Ala His Phe Gly Gly Asn
        195                 200                 205

Pro Asp Arg Val Thr Ile Phe Gly Glu Ser Ala Gly Gly Thr Ser Val
    210                 215                 220

Ser Ser Leu Val Val Ser Pro Ile Ser Gln Gly Leu Phe His Gly Ala
225                 230                 235                 240

Ile Met Glu Ser Gly Val Ala Leu Leu Pro Gly Leu Ile Ala Ser Ser
                245                 250                 255
```

```
Ala Asp Val Ile Ser Thr Val Val Ala Asn Leu Ser Ala Cys Asp Gln
            260                 265                 270

Val Asp Ser Glu Ala Leu Val Gly Cys Leu Arg Gly Lys Ser Lys Glu
        275                 280                 285

Glu Ile Leu Ala Ile Asn Lys Pro Phe Lys Met Ile Pro Gly Val Val
    290                 295                 300

Asp Gly Val Phe Leu Pro Arg His Pro Gln Glu Leu Leu Ala Ser Ala
305                 310                 315                 320

Asp Phe Gln Pro Val Pro Ser Ile Val Gly Val Asn Asn Asn Glu Phe
                325                 330                 335

Gly Trp Leu Ile Pro Lys Val Met Arg Ile Tyr Asp Thr Gln Lys Glu
            340                 345                 350

Met Asp Arg Glu Ala Ser Gln Ala Ala Leu Gln Lys Met Leu Thr Leu
        355                 360                 365

Leu Met Leu Pro Pro Thr Phe Gly Asp Leu Leu Arg Glu Glu Tyr Ile
    370                 375                 380

Gly Asp Asn Gly Asp Pro Gln Thr Leu Gln Ala Gln Phe Gln Glu Met
385                 390                 395                 400

Met Ala Asp Ser Met Phe Val Ile Pro Ala Leu Gln Val Ala His Phe
                405                 410                 415

Gln Cys Ser Arg Ala Pro Val Tyr Phe Tyr Glu Phe Gln His Gln Pro
            420                 425                 430

Ser Trp Leu Lys Asn Ile Arg Pro Pro His Met Lys Ala Asp His Gly
        435                 440                 445

Asp Glu Leu Pro Phe Val Phe Arg Ser Phe Phe Gly Gly Asn Tyr Ile
    450                 455                 460

Lys Phe Thr Glu Glu Glu Glu Gln Leu Ser Arg Lys Met Met Lys Tyr
465                 470                 475                 480

Trp Ala Asn Phe Ala Arg Asn Gly Asn Pro Asn Gly Glu Gly Leu Pro
                485                 490                 495

His Trp Pro Leu Phe Asp Gln Glu Glu Gln Tyr Leu Gln Leu Asn Leu
            500                 505                 510

Gln Pro Ala Val Gly Arg Ala Leu Lys Ala His Arg Leu Gln Phe Trp
        515                 520                 525
```

Lys Lys Ala Leu Pro Gln Lys Ile Gln Glu Leu Glu Glu Pro Glu Glu
530 535 540

Arg His Thr Glu Leu
545

<210> 690
<211> 155
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (36)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (46)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (50)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (85)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 690
Ser His Arg Val Thr His Cys Pro Tyr Ala Val Ala Leu Pro Glu Val
1 5 10 15

Ala Pro Ala Gln Pro Leu Thr Glu Ala Leu Arg Ala Leu Cys His Val
20 25 30

Gly Leu Phe Xaa Phe Ala Phe Cys Ala Leu Phe Asp Cys Xaa Arg Pro
35 40 45

Val Xaa Gln Lys Ser Cys Asp Leu Leu Leu Phe Leu Arg Asp Lys Ile
50 55 60

Ala Ser Tyr Ser Ser Leu Arg Glu Ala Arg Gly Ser Pro Asn Thr Ala
65 70 75 80

Ser Ala Glu Ala Xaa Leu Pro Arg Trp Arg Ala Gly Glu Gln Ala Gln
85 90 95

```
Pro Pro Gly Asp Gln Glu Pro Glu Ala Val Leu Ala Met Leu Arg Ser
            100                 105                 110

Leu Asp Leu Glu Gly Leu Arg Ser Thr Leu Ala Glu Ser Ser Asp His
        115                 120                 125

Val Glu Lys Ser Pro Gln Ser Leu Leu Gln Asp Met Leu Ala Thr Gly
    130                 135                 140

Gly Phe Leu Gln Gly Asp Glu Ala Asp Cys Tyr
145                 150                 155
```

<210> 691
<211> 149
<212> PRT
<213> Homo sapiens

<400> 691

```
Met Cys Leu Glu Arg Pro Leu Arg Glu Gly Pro Arg Val Met Glu Lys
  1               5                  10                  15

Glu Ala Trp Pro Gly Ser Leu Glu Gly Arg Gly Gly Gly Trp Arg His
             20                  25                  30

Leu Asp Cys Pro Leu Leu Ser His Thr Trp Gly Val Val Thr Pro Phe
         35                  40                  45

Thr Pro Ala Arg Leu Pro Ser Ala Phe His Glu Leu His Leu Leu Pro
     50                  55                  60

Thr Ser Leu Trp Arg Gly Trp Gly Pro Leu Ala Ser Thr Arg Gly Pro
 65                  70                  75                  80

Ser Ala Ser Pro Lys Pro Glu Pro Ser Ala Pro Gly Glu Asn Lys Trp
                 85                  90                  95

Leu Ser Phe Asp Thr Trp Gly Arg Arg Glu Ala Ala Gly Trp Arg Gln
            100                 105                 110

Ser Gln Gly Arg Asp Thr Thr Glu Gly Asp Pro Asp Ile Pro Arg Lys
        115                 120                 125

Phe Pro Ala Glu Gln Thr Ala Phe Gln Pro Glu Ala Cys Leu Asn Cys
    130                 135                 140

Val Met Cys Asn Asn
145
```

<210> 692
<211> 218
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (160)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 692
Pro Gly Val Lys Leu Trp Asp Val Pro Val Met Leu Asp His Lys Asp
1 5 10 15

Leu Glu Ala Glu Ile His Pro Leu Lys Asn Glu Glu Arg Lys Ser Gln
20 25 30

Glu Asn Leu Gly Asn Pro Ser Lys Asn Glu Asp Asn Val Lys Ser Ala
35 40 45

Pro Pro Gln Ser Arg Leu Ser Arg Cys Arg Ala Ala Ala Phe Phe Leu
50 55 60

Ser Leu Phe Leu Cys Leu Phe Val Val Phe Val Val Ser Phe Val Ile
65 70 75 80

Pro Cys Pro Asp Arg Pro Ala Ser Gln Arg Met Trp Arg Ile Asp Tyr
85 90 95

Ser Ala Ala Val Ile Tyr Asp Phe Leu Ala Val Asp Asp Ile Asn Gly
100 105 110

Asp Arg Ile Gln Asp Val Leu Phe Leu Tyr Lys Asn Thr Asn Ser Ser
115 120 125

Asn Asn Phe Ser Arg Ser Cys Val Asp Glu Gly Phe Ser Ser Pro Cys
130 135 140

Thr Phe Ala Ala Ala Val Ser Gly Ala Asn Ala Ala Arg Ser Gly Xaa
145 150 155 160

Asp Leu Trp Pro Lys Thr Trp Pro Ser Trp Ser Val Leu Cys Pro Ser
165 170 175

Gln Glu Ala Val Arg His Leu Leu Pro Ala Ser Trp Trp Ala Asp Pro
180 185 190

Val Leu Ser Leu Gln Ser Thr Cys Ser Gln Gly Lys Pro Trp Lys Pro
195 200 205

Gln Pro Ala Val Gln Gly Glu Trp Ser Ile
210 215

<210> 693
<211> 68
<212> PRT
<213> Homo sapiens

<400> 693
Ser Cys Asn Ser Ser Asn Asn Ile Leu Gln Leu Pro Tyr Arg Asn Arg
1 5 10 15

Ser Gly Arg Ala Lys Ser Asp Leu Gly Lys Val Ile Arg Tyr Arg Leu
20 25 30

Ser Ile Pro Phe Pro Lys Met Leu Gly Thr Arg Ser Ile Ser Asp Phe
35 40 45

Ile Ile Phe Phe Lys Val Trp Asn Ile Cys Ile Ile Leu Thr Ser Trp
50 55 60

Ala Ser Gln Ile
65

<210> 694
<211> 234
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (4)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (219)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 694
Cys Ala Xaa Xaa Leu Arg Gly Phe Asp Gln Gln Met Ser Ser Met Val

1 5 10 15

Ile Glu His Met Ala Ser His Gly Thr Arg Phe Leu Arg Gly Cys Ala
20 25 30

Pro Ser Arg Val Arg Arg Leu Pro Asp Gly Gln Leu Gln Val Thr Trp
35 40 45

Glu Asp Ser Thr Thr Gly Lys Glu Asp Thr Gly Thr Phe Asp Thr Val
50 55 60

Leu Trp Ala Ile Gly Arg Val Pro Asp Thr Arg Ser Leu Asn Leu Glu
65 70 75 80

Lys Ala Gly Val Asp Thr Ser Pro Asp Thr Gln Lys Ile Leu Val Asp
85 90 95

Ser Arg Glu Ala Thr Ser Val Pro His Ile Tyr Ala Ile Gly Asp Val
100 105 110

Val Glu Gly Arg Pro Glu Leu Thr Pro Thr Ala Ile Met Ala Gly Arg
115 120 125

Leu Leu Val Gln Arg Leu Phe Gly Gly Ser Ser Asp Leu Met Asp Tyr
130 135 140

Asp Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Val
145 150 155 160

Gly Leu Ser Glu Glu Glu Ala Val Ala Arg His Gly Gln Glu His Val
165 170 175

Glu Val Tyr His Ala His Tyr Lys Pro Leu Glu Phe Thr Val Ala Gly
180 185 190

Arg Asp Ala Ser Gln Cys Tyr Val Lys Met Val Cys Leu Arg Glu Pro
195 200 205

Pro Gln Leu Val Leu Gly Leu His Phe Leu Xaa Pro Thr Gln Ala Asn
210 215 220

Tyr Ser Arg Ile Cys Ser Gly Asp Lys Cys
225 230

<210> 695
<211> 460
<212> PRT
<213> Homo sapiens

<400> 695

```
Pro Cys Pro Pro Arg Pro Gln Glu Leu Pro Gly Arg Ser Pro Ser Ser
 1               5                  10                  15

Trp Ser Ala Leu Gly Trp Pro Ala Ala Leu Gly Gly Gly Val Val Ala
            20                  25                  30

Val Ala Val Cys Glu Pro Val Ala Arg Leu Leu Trp Ala Gly Thr Leu
        35                  40                  45

Lys Ile Ala Ala Met Ala Glu Asn Gly Asp Asn Glu Lys Met Ala Ala
    50                  55                  60

Leu Glu Ala Lys Ile Cys His Gln Ile Glu Tyr Tyr Phe Gly Asp Phe
65                  70                  75                  80

Asn Leu Pro Arg Asp Lys Phe Leu Lys Glu Gln Ile Lys Leu Asp Glu
                85                  90                  95

Gly Trp Val Pro Leu Glu Ile Met Ile Lys Phe Asn Arg Leu Asn Arg
            100                 105                 110

Leu Thr Thr Asp Phe Asn Val Ile Val Glu Ala Leu Ser Lys Ser Lys
        115                 120                 125

Ala Glu Leu Met Glu Ile Ser Glu Asp Lys Thr Lys Ile Arg Arg Ser
    130                 135                 140

Pro Ser Lys Pro Leu Pro Glu Val Thr Asp Glu Tyr Lys Asn Asp Val
145                 150                 155                 160

Lys Asn Arg Ser Val Tyr Ile Lys Gly Phe Pro Thr Asp Ala Thr Leu
                165                 170                 175

Asp Asp Ile Lys Glu Trp Leu Glu Asp Lys Gly Gln Val Leu Asn Ile
            180                 185                 190

Gln Met Arg Arg Thr Leu His Lys Ala Phe Lys Gly Ser Ile Phe Val
        195                 200                 205

Val Phe Asp Ser Ile Glu Ser Ala Lys Lys Phe Val Glu Thr Pro Gly
    210                 215                 220

Gln Lys Tyr Lys Glu Thr Asp Leu Leu Ile Leu Phe Lys Asp Asp Tyr
225                 230                 235                 240

Phe Ala Lys Lys Asn Glu Glu Arg Lys Gln Asn Lys Val Glu Ala Lys
                245                 250                 255

Leu Arg Ala Lys Gln Glu Gln Glu Ala Lys Gln Lys Leu Glu Glu Asp
            260                 265                 270
```

Ala Glu Met Lys Ser Leu Glu Glu Lys Ile Gly Cys Leu Leu Lys Phe
275 280 285

Ser Gly Asp Leu Asp Asp Gln Thr Cys Arg Glu Asp Leu His Ile Leu
290 295 300

Phe Ser Asn His Gly Glu Ile Lys Trp Ile Asp Phe Val Arg Gly Ala
305 310 315 320

Lys Glu Gly Ile Ile Leu Phe Lys Glu Lys Ala Lys Glu Ala Leu Gly
325 330 335

Lys Ala Lys Asp Ala Asn Asn Gly Asn Leu Gln Leu Arg Asn Lys Glu
340 345 350

Val Thr Trp Glu Val Leu Glu Gly Glu Val Glu Lys Glu Ala Leu Lys
355 360 365

Lys Ile Ile Glu Asp Gln Gln Glu Ser Leu Asn Lys Trp Lys Ser Lys
370 375 380

Gly Arg Arg Phe Lys Gly Lys Gly Lys Gly Asn Lys Ala Ala Gln Pro
385 390 395 400

Gly Ser Gly Lys Gly Lys Val Gln Phe Gln Gly Lys Lys Thr Lys Phe
405 410 415

Ala Ser Asp Asp Glu His Asp Glu His Asp Glu Asn Gly Ala Thr Gly
420 425 430

Pro Val Lys Arg Ala Arg Glu Glu Thr Asp Lys Glu Glu Pro Ala Ser
435 440 445

Lys Gln Gln Lys Thr Glu Asn Gly Ala Gly Asp Gln
450 455 460

<210> 696
<211> 80
<212> PRT
<213> Homo sapiens

<400> 696
Gly Glu Glu Gly Val Gly Ser Pro Ser Gly Ile Leu Ala Thr Pro Leu
1 5 10 15

Arg Ser Ala Arg Gly Thr Thr His Thr His Thr His Thr His Thr His
20 25 30

Thr His Ser His Thr His Ala His Phe Pro Ser Phe Pro Asp Pro Leu
35 40 45

Phe Gln Ser Ser Pro Phe Ser Ser Gly Phe Ile Asp Glu Tyr Lys Tyr
50 55 60

Pro His Leu Trp Pro Val Met Ser Val Thr Cys Cys Arg Phe Cys Val
65 70 75 80

<210> 697
<211> 257
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 697
Trp Pro Arg Arg Pro Gly Pro His Leu Gly Val Leu Glu Phe Pro Gly
1 5 10 15

Ala Gly Cys Gly Ala Ser Ala Ala Gly Trp Pro Ser Ala Xaa Met Leu
20 25 30

Pro Gly Arg Gly Pro Arg Pro Phe Arg Ala Arg Leu Val Gly Arg Glu
35 40 45

Leu Val Ser Met Leu Ala Arg Glu Leu Pro Ala Ala Val Ala Pro Ala
50 55 60

Gly Pro Ala Ser Leu Ala Arg Trp Thr Leu Gly Phe Cys Asp Glu Arg
65 70 75 80

Leu Val Pro Phe Asp His Ala Glu Ser Thr Tyr Gly Leu Tyr Arg Thr
85 90 95

His Leu Leu Ser Arg Leu Pro Ile Pro Glu Ser Gln Val Ile Thr Ile
100 105 110

Asn Pro Glu Leu Pro Val Glu Glu Ala Ala Glu Asp Tyr Ala Lys Lys
115 120 125

Leu Arg Gln Ala Phe Gln Gly Asp Ser Ile Pro Val Phe Asp Leu Leu
130 135 140

Ile Leu Gly Val Gly Pro Asp Gly His Thr Cys Ser Leu Phe Pro Asp
145 150 155 160

His Pro Leu Leu Gln Glu Arg Glu Lys Ile Val Ala Pro Ile Ser Asp
165 170 175

Ser Pro Lys Pro Pro Pro Gln Arg Val Thr Leu Thr Leu Pro Val Leu
180 185 190

Asn Ala Ala Arg Thr Val Ile Phe Val Ala Thr Gly Glu Gly Lys Ala
195 200 205

Ala Val Leu Lys Arg Ile Leu Glu Asp Gln Glu Glu Asn Pro Leu Pro
210 215 220

Ala Ala Leu Val Gln Pro His Thr Gly Lys Leu Cys Trp Phe Leu Asp
225 230 235 240

Glu Ala Ala Ala Arg Leu Leu Thr Val Pro Phe Glu Lys His Ser Thr
245 250 255

Leu

<210> 698
<211> 68
<212> PRT
<213> Homo sapiens

<400> 698
Gln Tyr Lys Thr Pro Ala Val Asp Thr Thr Met Met Thr Phe His Glu
1 5 10 15

Leu Val Phe Leu Val Leu Thr Ala Lys Phe Val Leu Phe Thr Gly Gln
20 25 30

Ile Ser Asn Lys Val Leu Gly Leu Lys Ile His Gly Trp Thr Glu Val
35 40 45

Pro Tyr Pro Leu Thr Met Glu Ala Gly Ala Thr Phe Trp Gly Tyr Leu
50 55 60

Phe Leu Asn Phe
65

<210> 699

<211> 360
<212> PRT
<213> Homo sapiens

<400> 699

```
Pro Cys Ser Ala Thr Thr Ala Trp Val Lys Ser Ser Ile Lys Thr His
  1               5                  10                  15

Leu Cys Ala Ser Leu Arg His Ile Arg Phe Leu Leu Ser Val Cys Leu
             20                  25                  30

Leu Cys Leu Val Ala Gly Thr Ala Val Ala Val Lys Met Ala Ser Thr
         35                  40                  45

Ser Arg Leu Asp Ala Leu Pro Arg Val Thr Cys Pro Asn His Pro Asp
     50                  55                  60

Ala Ile Leu Val Glu Asp Tyr Arg Ala Gly Asp Met Ile Cys Pro Glu
 65                  70                  75                  80

Cys Gly Leu Val Val Gly Asp Arg Val Ile Asp Val Gly Ser Glu Trp
                 85                  90                  95

Arg Thr Phe Ser Asn Asp Lys Ala Thr Lys Asp Pro Ser Arg Val Gly
            100                 105                 110

Asp Ser Gln Asn Pro Leu Leu Ser Asp Gly Asp Leu Ser Thr Met Ile
        115                 120                 125

Gly Lys Gly Thr Gly Ala Ala Ser Phe Asp Glu Phe Gly Asn Ser Lys
    130                 135                 140

Tyr Gln Asn Arg Arg Thr Met Ser Ser Ser Asp Arg Ala Met Met Asn
145                 150                 155                 160

Ala Phe Lys Glu Ile Thr Thr Met Ala Asp Arg Ile Asn Leu Pro Arg
                165                 170                 175

Asn Ile Val Asp Arg Thr Asn Asn Leu Phe Lys Gln Val Tyr Glu Gln
            180                 185                 190

Lys Ser Leu Lys Gly Arg Ala Asn Asp Ala Ile Ala Ser Ala Cys Leu
        195                 200                 205

Tyr Ile Ala Cys Arg Gln Glu Gly Val Pro Arg Thr Phe Lys Glu Ile
    210                 215                 220

Cys Ala Val Ser Arg Ile Ser Lys Lys Glu Ile Gly Arg Cys Phe Lys
225                 230                 235                 240

Leu Ile Leu Lys Ala Leu Glu Thr Ser Val Asp Leu Ile Thr Thr Gly
```

```
                245                 250                 255

Asp Phe Met Ser Arg Phe Cys Ser Asn Leu Cys Leu Pro Lys Gln Val
            260                 265                 270

Gln Met Ala Ala Thr His Ile Ala Arg Lys Ala Val Glu Leu Asp Leu
        275                 280                 285

Val Pro Gly Arg Ser Pro Ile Ser Val Ala Ala Ala Ala Ile Tyr Met
    290                 295                 300

Ala Ser Gln Ala Ser Ala Glu Lys Arg Thr Gln Lys Glu Ile Gly Asp
305                 310                 315                 320

Ile Ala Gly Val Ala Asp Val Thr Ile Arg Gln Ser Tyr Arg Leu Ile
                325                 330                 335

Tyr Pro Arg Ala Pro Asp Leu Phe Pro Thr Asp Phe Lys Phe Asp Thr
            340                 345                 350

Pro Val Asp Lys Leu Pro Gln Leu
        355                 360
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<210> 700
<211> 364
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (13)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (353)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (360)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 700

Pro Ser Trp Leu Arg Ala Arg Ser Ser Arg Ser Trp Xaa Ala Ser Pro
1   5   10   15

Arg Gly Pro Gln Pro Pro Arg Ile Arg Ala Arg Ser Ala Xaa Pro Met
            20   25   30

Glu Gly Ala Arg Val Phe Gly Ala Leu Gly Pro Ile Gly Pro Ser Ser
        35   40   45

Pro Gly Leu Thr Leu Gly Gly Leu Ala Val Ser Glu His Arg Leu Ser
    50   55   60

Asn Lys Leu Leu Ala Trp Ser Gly Val Leu Glu Trp Gln Glu Lys Arg
65   70   75   80

Arg Pro Tyr Ser Asp Ser Thr Ala Lys Leu Lys Arg Thr Leu Pro Cys
                85   90   95

Gln Ala Tyr Val Asn Gln Gly Glu Asn Leu Glu Thr Asp Gln Trp Pro
            100   105   110

Gln Lys Leu Ile Met Gln Leu Ile Pro Gln Gln Leu Leu Thr Thr Leu
        115   120   125

Gly Pro Leu Phe Arg Asn Ser Gln Leu Ala Gln Phe His Phe Thr Asn
    130   135   140

Arg Asp Cys Asp Ser Leu Lys Gly Leu Cys Arg Ile Met Gly Asn Gly
145   150   155   160

Phe Ala Gly Cys Met Leu Phe Pro His Ile Ser Pro Cys Glu Val Arg
                165   170   175

Val Leu Met Leu Leu Tyr Ser Ser Lys Lys Lys Ile Phe Met Gly Leu
            180   185   190

Ile Pro Tyr Asp Gln Ser Gly Phe Val Ser Ala Ile Arg Gln Val Ile
        195   200   205

Thr Thr Arg Lys Gln Ala Val Gly Pro Gly Gly Val Asn Ser Gly Pro
    210   215   220

Val Gln Ile Val Asn Asn Lys Phe Leu Ala Trp Ser Gly Val Met Glu
225   230   235   240

Trp Gln Glu Pro Arg Pro Glu Pro Asn Ser Arg Ser Lys Arg Trp Leu
                245   250   255

Pro Ser His Val Tyr Val Asn Gln Gly Glu Ile Leu Arg Thr Glu Gln
            260   265   270

Trp Pro Arg Lys Leu Tyr Met Gln Leu Ile Pro Gln Gln Leu Leu Thr
275 280 285

Thr Leu Val Pro Leu Phe Arg Asn Ser Arg Leu Val Gln Phe His Phe
290 295 300

Thr Lys Asp Leu Glu Thr Leu Lys Ser Leu Cys Arg Ile Met Asp Asn
305 310 315 320

Gly Phe Ala Gly Cys Val His Phe Ser Tyr Lys Ala Ser Cys Glu Ile
325 330 335

Arg Val Leu Met Leu Leu Tyr Ser Ser Glu Lys Lys Ile Phe Ile Gly
340 345 350

Xaa Ile Pro His Asp Gln Gly Xaa Phe Val Gln Arg
355 360

<210> 701
<211> 156
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (33)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 701
Gly Thr Arg Gly Ile Leu His Val Ala Val Pro Ala Arg Gly Thr His
1 5 10 15

Ala Gln Cys Cys Arg Asn Trp Thr Val Pro Asp Ser Gly Gln Gly Lys
20 25 30

Xaa Val Met Leu Glu Gly Gln Gly Arg Leu Glu Arg Val His Ile Pro
35 40 45

Leu Ser Ala Pro Ala Ser Ala Thr Val Gln Arg Pro Thr Gly Pro Gln
50 55 60

Pro Val Ala Cys Pro His Cys Pro Val Pro Thr Ser Asn Ser Pro Gln
65 70 75 80

Pro Leu Val Ala Ser Val Pro Cys Pro Leu Gly Phe Ser Ser Gln Pro
85 90 95

Ser Gly Leu Gly Leu Cys Arg Lys Val Met Pro Thr Gly Thr Leu Leu
100 105 110

Thr Pro Gly Ser Phe Met Asp Val Val Ser Glu Leu Arg Thr Arg Gly
115 120 125

Cys Gln Met Phe Leu Ala Pro His Val Ser Phe Arg Thr Glu Gln Lys
130 135 140

His Lys Asp Ser Ala Lys Ser Ser Leu Tyr Ser Leu
145 150 155

<210> 702
<211> 150
<212> PRT
<213> Homo sapiens

<400> 702
Ala Gly His Gly Leu Gly Val Arg Ala Gly Leu Lys Glu Phe Ala Thr
1 5 10 15

Asn Leu Thr Glu Ser Gly Val His Gly Ala Leu Leu Ala Leu Asp Glu
20 25 30

Thr Phe Asp Tyr Ser Asp Leu Ala Leu Leu Leu Gln Ile Pro Thr Gln
35 40 45

Asn Ala Gln Ala Arg Gln Leu Leu Glu Lys Glu Phe Ser Asn Leu Ile
50 55 60

Ser Leu Gly Thr Asp Arg Arg Leu Asp Glu Asp Ser Ala Lys Ser Phe
65 70 75 80

Ser Arg Ser Pro Ser Trp Arg Lys Met Phe Arg Glu Lys Asp Leu Arg
85 90 95

Gly Val Thr Pro Asp Ser Ala Glu Met Leu Pro Pro Asn Phe Arg Ser
100 105 110

Ala Ala Ala Gly Ala Leu Gly Ser Pro Gly Leu Pro Leu Arg Lys Leu
115 120 125

Gln Pro Glu Gly Gln Thr Ser Gly Ser Ser Arg Ala Asp Gly Val Ser
130 135 140

Val Arg Thr Tyr Ser Cys
145 150

<210> 703

<211> 527
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (243)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (257)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (259)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (471)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (477)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (480)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (484)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (511)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (519)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 703
Cys Val Cys Val Glu Gly Val Glu Gly Pro Arg Cys Asp Lys Cys Thr

1 5 10 15

Arg Gly Tyr Ser Gly Val Phe Pro Asp Cys Thr Pro Cys His Gln Cys
20 25 30

Phe Ala Leu Trp Asp Val Ile Ile Ala Glu Leu Thr Asn Arg Thr His
35 40 45

Arg Phe Leu Glu Lys Ala Lys Ala Leu Lys Ile Ser Gly Val Ile Gly
50 55 60

Pro Tyr Arg Glu Thr Val Asp Ser Val Glu Arg Lys Val Ser Glu Ile
65 70 75 80

Lys Asp Ile Leu Ala Gln Ser Pro Ala Ala Glu Pro Leu Lys Asn Ile
85 90 95

Gly Asn Leu Phe Glu Glu Ala Glu Lys Leu Ile Lys Asp Val Thr Glu
100 105 110

Met Met Ala Gln Val Glu Val Lys Leu Ser Asp Thr Thr Ser Gln Ser
115 120 125

Asn Ser Thr Ala Lys Glu Leu Asp Ser Leu Gln Thr Glu Ala Glu Ser
130 135 140

Leu Asp Asn Thr Val Lys Glu Leu Ala Glu Gln Leu Glu Phe Ile Lys
145 150 155 160

Asn Ser Asp Ile Arg Gly Ala Leu Asp Ser Ile Thr Lys Tyr Phe Gln
165 170 175

Met Ser Leu Glu Ala Glu Glu Arg Val Asn Ala Ser Thr Thr Glu Pro
180 185 190

Asn Ser Thr Val Glu Gln Ser Ala Leu Met Arg Asp Arg Val Glu Asp
195 200 205

Val Met Met Glu Arg Glu Ser Gln Phe Lys Glu Lys Gln Glu Glu Gln
210 215 220

Ala Arg Leu Leu Asp Glu Leu Ala Gly Lys Leu Gln Ser Leu Asp Leu
225 230 235 240

Ser Ala Xaa Ala Glu Met Thr Cys Gly Thr Pro Pro Gly Ala Ser Cys
245 250 255

Xaa Glu Xaa Glu Cys Gly Gly Pro Asn Cys Arg Thr Asp Glu Gly Glu
260 265 270

Arg Lys Cys Gly Gly Pro Gly Cys Gly Gly Leu Val Thr Val Ala His

275 280 285

Asn Ala Trp Gln Lys Ala Met Asp Leu Asp Gln Asp Val Leu Ser Ala
290 295 300

Leu Ala Glu Val Glu Gln Leu Ser Lys Met Val Ser Glu Ala Lys Leu
305 310 315 320

Arg Ala Asp Glu Ala Lys Gln Ser Ala Glu Asp Ile Leu Leu Lys Thr
325 330 335

Asn Ala Thr Lys Glu Lys Met Asp Lys Ser Asn Glu Glu Leu Arg Asn
340 345 350

Leu Ile Lys Gln Ile Arg Asn Phe Leu Thr Gln Asp Ser Ala Asp Leu
355 360 365

Asp Ser Ile Glu Ala Val Ala Asn Glu Val Leu Lys Met Glu Met Pro
370 375 380

Ser Thr Pro Gln Gln Leu Gln Asn Leu Thr Glu Asp Ile Arg Glu Arg
385 390 395 400

Val Glu Ser Leu Ser Gln Val Glu Val Ile Leu Gln His Ser Ala Ala
405 410 415

Asp Ile Ala Arg Ala Glu Met Leu Leu Glu Glu Ala Lys Arg Ala Ser
420 425 430

Lys Ser Ala Thr Asp Val Lys Val Thr Ala Asp Met Val Lys Glu Ala
435 440 445

Leu Glu Glu Ala Glu Lys Ala Gln Val Ala Ala Glu Lys Ala Ile Lys
450 455 460

Gln Ala Asp Glu Asp Ile Xaa Arg Asn Pro Glu Pro Xaa Asn Phe Xaa
465 470 475 480

Leu Glu Phe Xaa Lys Gln Gln Leu Ser Gly Gly Asn Leu Val Gln Arg
485 490 495

Val Pro Arg Ala Ser Ser Glu Phe Arg Glu Asp Val Gly Arg Xaa Leu
500 505 510

Ser Gly Lys Leu Ala Gln Xaa Pro Gly Gly Gly Arg Ile Phe Trp
515 520 525

<210> 704
<211> 62

<212> PRT
<213> Homo sapiens

<400> 704
Val Tyr Gln Arg Lys Ser Thr Val Val Leu Gly Gly Phe Leu Leu Trp
1 5 10 15

Asp Ile Asp Phe Leu Phe Phe Phe Arg Asn Ile Val Cys Cys Asn Leu
20 25 30

Asn Lys Asn Tyr Asp Ile Leu Arg Tyr Phe Ile Asp Lys Pro Asn Lys
35 40 45

Asn Ile Cys Phe Tyr Phe Lys Val Asn Val Phe Leu Phe Ser
50 55 60

<210> 705
<211> 44
<212> PRT
<213> Homo sapiens

<400> 705
Thr Glu Asp Leu Phe Gly Phe Lys His Leu Leu Arg Gln Tyr Leu Leu
1 5 10 15

Gly Lys Pro Asn Ile Ala Asn Gly Gln Phe Asp Phe Asn Phe Ser Lys
20 25 30

Asp Thr Leu Leu Ser Arg Arg Leu Lys Cys Leu His
35 40

<210> 706
<211> 193
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 706
Xaa Gly Arg Ala Trp Val Met Ala Ala Pro Gly Ala Leu Leu Val Met
1 5 10 15

Gly Val Ser Gly Ser Gly Lys Ser Thr Val Gly Ala Leu Leu Ala Ser
20 25 30

Glu Leu Gly Trp Lys Phe Tyr Asp Ala Asp Asp Tyr His Pro Glu Glu
35 40 45

Asn Arg Arg Lys Met Gly Lys Gly Ile Pro Leu Asn Asp Gln Asp Arg
50 55 60

Ile Pro Trp Leu Cys Asn Leu His Asp Ile Leu Leu Arg Asp Val Ala
65 70 75 80

Ser Gly Gln Arg Val Val Leu Ala Cys Ser Ala Leu Lys Lys Thr Tyr
85 90 95

Arg Asp Ile Leu Thr Gln Gly Lys Asp Gly Val Ala Leu Lys Cys Glu
100 105 110

Glu Ser Gly Lys Glu Ala Lys Gln Ala Glu Met Gln Leu Leu Val Val
115 120 125

His Leu Ser Gly Ser Phe Glu Val Ile Ser Gly Arg Leu Leu Lys Arg
130 135 140

Glu Gly His Phe Met Pro Pro Glu Leu Leu Gln Ser Gln Phe Glu Thr
145 150 155 160

Leu Glu Pro Pro Ala Ala Pro Glu Asn Phe Ile Gln Ile Ser Val Asp
165 170 175

Lys Asn Val Ser Glu Ile Ile Ala Thr Ile Met Glu Thr Leu Lys Met
180 185 190

Lys

<210> 707
<211> 121
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (102)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (103)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 707
Gly Ile Arg Gly Gln Thr Leu Trp Leu Gly Pro Leu Gly Ala Thr Leu
1 5 10 15

Trp Pro Leu Gly Ala Leu Glu Thr Ser His Val Leu Trp Ala Leu Trp
20 25 30

Arg Ala Leu Ala Leu His Gly Gly Ala Gly Arg His Cys Leu Pro Cys
35 40 45

Pro Leu Pro Ala Ala Pro Ala Leu Val Cys Arg Leu Gly Pro Gly Cys
50 55 60

Leu Leu Leu Gly Val Trp Pro Arg Ala Pro Val Lys Pro Trp Arg His
65 70 75 80

Cys Val Cys Val Met Gly Ser Glu Gly Leu Val Gly Ala Val His Trp
85 90 95

Ser Ser Ser Leu Pro Xaa Xaa Ala Ile Ser Met Ala Pro Phe Ala Ala
100 105 110

Glu Asp Thr His Cys Gly Ser Val Gly
115 120

<210> 708
<211> 112
<212> PRT
<213> Homo sapiens

<400> 708
Asn Ser Phe Cys Tyr Phe His Ile Arg Val Gln Thr Tyr Lys Gly Ala
1 5 10 15

Cys Ser Leu Lys Val His Asn Tyr Ser Tyr Ser Val Cys Leu Tyr Cys
20 25 30

Tyr Arg Met Leu Cys Phe Gly Ala Leu Ser Ser Ala Asp Pro Arg Ser
35 40 45

Ser Val Glu Ile His Cys Leu Gly His Ser Leu Ile Arg Met Leu Ala
50 55 60

Gly Asp Phe Val Ser Asp Val Ala Ser Leu Phe Ser Val His Arg Leu
65 70 75 80

Arg Val Thr Thr Val Ala Cys Arg Val His Pro Val Gly Ala Ala Gln
85 90 95

Leu Ser Glu Ser Lys Asn Leu Pro Thr Tyr Ser Asn Val Phe Ala Leu
100 105 110

<210> 709
<211> 72
<212> PRT
<213> Homo sapiens

<400> 709
Arg Arg Val Trp Val Leu Phe Pro Pro Gln Arg Pro Glu Ser Gly Trp
1 5 10 15

Gly Val Ser Pro Val Glu Gly Glu Thr Val Pro Ala Leu Arg Gly Met
20 25 30

Lys Lys Ser Val Gly Leu Pro Val Ala Val Gln Cys Val Ala Leu Pro
35 40 45

Trp Gln Glu Glu Leu Cys Leu Arg Phe Met Arg Glu Val Glu Arg Leu
50 55 60

Met Thr Pro Glu Lys Gln Ser Ser
65 70

<210> 710
<211> 84
<212> PRT
<213> Homo sapiens

<400> 710
Arg Leu His Arg Tyr Pro Glu Ala Met Ala Ser Lys Gly Leu Gln Asp
1 5 10 15

Leu Lys Gln Gln Val Glu Gly Thr Ala Gln Glu Ala Val Ser Ala Ala
20 25 30

Gly Ala Ala Ala Gln Gln Val Val Asp Gln Ala Thr Glu Ala Gly Gln
35 40 45

Lys Ala Met Asp Gln Leu Ala Lys Thr Thr Gln Glu Thr Ile Asp Lys
50 55 60

Thr Ala Asn Gln Ala Ser Asp Thr Phe Ser Gly Ile Gly Lys Lys Phe
65 70 75 80

Gly Leu Leu Lys

<210> 711
<211> 63
<212> PRT
<213> Homo sapiens

<400> 711
Arg Leu His Arg Tyr Pro Glu Ala Met Ala Ser Lys Gly Leu Gln Asp
1 5 10 15

Leu Lys Gln Gln Val Glu Gly Thr Ala Gln Glu Ala Ala Met Asp Gln
20 25 30

Leu Ala Lys Thr Thr Gln Glu Thr Ile Asp Lys Thr Ala Asn Gln Ala
35 40 45

Ser Asp Thr Phe Ser Gly Ile Gly Lys Lys Phe Gly Leu Leu Lys
50 55 60

<210> 712
<211> 86
<212> PRT
<213> Homo sapiens

<400> 712
Arg Leu Ala Asn Arg Ala Ile Met Ser His Lys Gln Ile Tyr Tyr Ser
1 5 10 15

Asp Lys Tyr Asp Asp Glu Glu Phe Glu Tyr Arg His Val Met Leu Pro
20 25 30

Lys Asp Ile Ala Lys Leu Val Pro Lys Thr His Leu Met Ser Glu Ser
35 40 45

Glu Trp Arg Asn Leu Gly Val Gln Gln Ser Gln Gly Trp Val His Tyr
50 55 60

Met Ile His Glu Pro Glu Pro His Ile Leu Leu Phe Arg Arg Pro Leu
65 70 75 80

Pro Lys Lys Pro Lys Lys
85

<210> 713
<211> 193
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (129)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 713
```
Val Gln Lys Ala Gly Ala Arg Ala Leu Ala Val Ala Gly Ala Ala Arg
 1               5                  10                  15

Thr Pro Arg Ser Leu Pro Gly Arg Pro Ala Val Cys Asn Met Thr Leu
            20                  25                  30

Glu Glu Phe Ser Ala Gly Glu Gln Lys Thr Glu Arg Met Asp Lys Val
        35                  40                  45

Gly Asp Ala Leu Glu Glu Val Leu Ser Lys Ala Leu Ser Gln Arg Thr
    50                  55                  60

Ile Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn Val Asp Pro
65                  70                  75                  80

Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp Asp Asp Arg
                85                  90                  95

Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ala Phe Cys Cys
            100                 105                 110

Glu Asn Asp Ile Asn Ile Leu Arg Val Thr Thr Arg Ala Gly Trp Arg
        115                 120                 125

Xaa Pro Ala Leu Gly Asp Arg Arg Trp Pro Arg Gly Glu Arg Gly Arg
    130                 135                 140

Arg Ala Ala Pro Gly Pro Ala Leu Arg Val Val Thr Asn Pro His Ser
145                 150                 155                 160

Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile Cys Phe Cys Arg
                165                 170                 175

Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile Asn Leu Pro Glu
            180                 185                 190

Arg
```

<210> 714
<211> 200
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (93)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (190)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 714
```
Gly Pro Gly Ala Cys Ser Gly Pro Ala Pro Ser Pro Arg Arg Pro Gln
 1               5                  10                  15

Ser Val Lys Cys Glu Pro Arg Arg Arg Gly Arg Ile Trp Pro Gly Ala
            20                  25                  30

Gly Gly Gly Val Gly Ala Ala Arg His Val His His His Gln Gly Ala
        35                  40                  45

Gln Gln Ala Gly Arg Ala Ala Pro His Arg Ser His Ala Ala Ala Gly
    50                  55                  60

Gly Gly Pro Ala Arg Arg Ala Pro Glu Met Pro Ala Ala Arg Ala Ala
65                  70                  75                  80

Asp Leu Ala Ala Pro Ala Gly Ala Ala Xaa Cys Ala Xaa Pro Gly Pro
                85                  90                  95

Trp Pro Leu Ser Ser Pro Gly Pro Arg Leu Val Phe Asn Arg Val Asn
            100                 105                 110

Gly Arg Arg Ala Pro Ser Thr Ser Pro Ser Phe Glu Gly Thr Gln Glu
        115                 120                 125

Thr Tyr Thr Val Ala His Glu Glu Asn Val Arg Phe Val Ser Glu Ala
    130                 135                 140

Trp Gln Gln Val Gln Gln Gln Leu Asp Gly Gly Pro Ala Gly Glu Gly
```

145 150 155 160

Gly Pro Arg Pro Val Gln Tyr Val Glu Arg Thr Pro Asn Pro Arg Leu
165 170 175

Gln Asn Phe Val Pro Ile Asp Leu Asp Glu Trp Trp Ala Xaa Gln Phe
180 185 190

Leu Ala Arg Ile Thr Ser Cys Ser
195 200

<210> 715
<211> 106
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 715
Trp Ile Pro Arg Ala Ala Gly Ile Arg His Glu Leu Val Pro Xaa Leu
1 5 10 15

Trp Ser Arg Glu Glu Ala Met Ala Thr Met Glu Asn Lys Val Ile Cys
20 25 30

Ala Leu Val Leu Val Ser Met Leu Ala Leu Gly Thr Leu Ala Glu Ala
35 40 45

Gln Thr Glu Thr Cys Thr Val Ala Pro Arg Glu Arg Gln Asn Cys Gly
50 55 60

Phe Pro Gly Val Thr Pro Ser Gln Cys Ala Asn Lys Gly Cys Cys Phe
65 70 75 80

Asp Asp Thr Val Arg Gly Val Pro Trp Cys Phe Tyr Pro Asn Thr Ile
85 90 95

Asp Val Pro Pro Glu Glu Glu Cys Glu Phe
100 105

<210> 716
<211> 105
<212> PRT
<213> Homo sapiens

<400> 716

Glu Gly Arg Glu Ala Gly Ser Gly Leu Ser Val Asp Ser Arg Asp Lys
1 5 10 15

Gly His Glu Gly Arg Gly Leu Gly Pro Phe Arg Ile Pro Gln Asp Ser
20 25 30

Gln Val Gln Leu Cys Gln Lys Gly Thr Phe His Val Met Gln Leu Arg
35 40 45

Gly Leu Ser Leu Asn Pro Arg Leu Leu Leu Thr Leu Gly Ser Phe Asn
50 55 60

Gln Val Gly Gln Pro Leu Leu Gln Arg Gly Val Gly Trp Leu Ser Ser
65 70 75 80

Leu Ser His Ala Ala Cys Glu Asp Arg Gly Gly Gly Val Gly Ser Gly
85 90 95

Lys Ser Pro Glu Asn Arg Arg Gly Ile
100 105

<210> 717
<211> 431
<212> PRT
<213> Homo sapiens

<400> 717

Arg Ala Ala Gly Ile Arg His Glu Arg Gly Gly Pro Thr Gly Ser Cys
1 5 10 15

Pro Gly Leu Pro Ser Pro Pro Met Val Leu Tyr Ile Lys Tyr Pro Gly
20 25 30

Trp Arg Ser His Met Leu Leu Thr Glu Gly Gly Asn Tyr His Ser Ser
35 40 45

Leu Gly Thr Arg Cys Glu Leu Ser Cys Asp Arg Gly Phe Arg Leu Ile
50 55 60

Gly Arg Arg Ser Val Gln Cys Leu Pro Ser Arg Arg Trp Ser Gly Thr
65 70 75 80

Ala Tyr Cys Arg Gln Met Arg Cys His Ala Leu Pro Phe Ile Thr Ser
85 90 95

Gly Thr Tyr Thr Cys Thr Asn Gly Val Leu Leu Asp Ser Arg Cys Asp
100 105 110

```
Tyr Ser Cys Ser Ser Gly Tyr His Leu Glu Gly Asp Arg Ser Arg Ile
        115                 120                 125

Cys Met Glu Asp Gly Arg Trp Ser Gly Gly Glu Pro Val Cys Val Asp
    130                 135                 140

Ile Asp Pro Pro Lys Ile Arg Cys Pro His Ser Arg Glu Lys Met Ala
145                 150                 155                 160

Glu Pro Glu Lys Leu Thr Ala Arg Val Tyr Trp Asp Pro Pro Leu Val
                165                 170                 175

Lys Asp Ser Ala Asp Gly Thr Ile Thr Arg Val Thr Leu Arg Gly Pro
            180                 185                 190

Glu Pro Gly Ser His Phe Pro Glu Gly Glu His Val Ile Arg Tyr Thr
        195                 200                 205

Ala Tyr Asp Arg Ala Tyr Asn Arg Ala Ser Cys Lys Phe Ile Val Lys
    210                 215                 220

Val Gln Val Arg Arg Cys Pro Thr Leu Lys Pro Pro Gln His Gly Tyr
225                 230                 235                 240

Leu Thr Cys Thr Ser Ala Gly Asp Asn Tyr Gly Ala Thr Cys Glu Tyr
                245                 250                 255

His Cys Asp Gly Gly Tyr Asp Arg Gln Gly Thr Pro Ser Arg Val Cys
            260                 265                 270

Gln Ser Ser Arg Gln Trp Ser Gly Ser Pro Pro Ile Cys Ala Pro Met
        275                 280                 285

Lys Ile Asn Val Asn Val Asn Ser Ala Ala Gly Leu Leu Asp Gln Phe
    290                 295                 300

Tyr Glu Lys Gln Arg Leu Leu Ile Ile Ser Ala Pro Asp Pro Ser Asn
305                 310                 315                 320

Arg Tyr Tyr Lys Met Gln Ile Ser Met Leu Gln Gln Ser Thr Cys Gly
                325                 330                 335

Leu Asp Leu Arg His Val Thr Ile Ile Glu Leu Val Gly Gln Pro Pro
            340                 345                 350

Gln Glu Val Gly Arg Ile Arg Glu Gln Gln Leu Ser Ala Asn Ile Ile
        355                 360                 365

Glu Glu Leu Arg Gln Phe Gln Arg Leu Thr Arg Ser Tyr Phe Asn Met
    370                 375                 380
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Val Leu Ile Asp Lys Gln Gly Ile Asp Arg Asp Arg Tyr Met Glu Pro
385                 390                 395                 400

Val Thr Pro Glu Glu Ile Phe Thr Phe Ile Asp Asp Tyr Leu Leu Ser
                405                 410                 415

Asn Gln Glu Leu Thr Gln Arg Arg Glu Gln Arg Asp Ile Cys Glu
            420                 425                 430


<210> 718
<211> 417
<212> PRT
<213> Homo sapiens

<400> 718
Gln Gly Leu Pro Asp Gly Val Trp Ala His Gly Thr Cys Pro Gly His
  1               5                  10                  15

Arg Leu Val Ser Ser Gln Arg Arg Ile Ile Ala Ser Gly Ser Glu Asp
            20                  25                  30

Cys Thr Val Met Val Trp Gln Ile Pro Glu Asn Gly Leu Thr Ser Pro
        35                  40                  45

Leu Thr Glu Pro Val Val Val Leu Glu Gly His Thr Lys Arg Val Gly
    50                  55                  60

Ile Ile Ala Trp His Pro Thr Ala Arg Asn Val Leu Leu Ser Ala Gly
 65                  70                  75                  80

Cys Asp Asn Val Val Leu Ile Trp Asn Val Gly Thr Ala Glu Glu Leu
                85                  90                  95

Tyr Arg Leu Asp Ser Leu His Pro Asp Leu Ile Tyr Asn Val Ser Trp
            100                 105                 110

Asn His Asn Gly Ser Leu Phe Cys Ser Ala Cys Lys Asp Lys Ser Val
        115                 120                 125

Arg Ile Ile Asp Pro Arg Arg Gly Thr Leu Val Ala Glu Arg Glu Lys
    130                 135                 140

Ala His Glu Gly Ala Arg Pro Met Arg Ala Ile Phe Leu Ala Asp Gly
145                 150                 155                 160

Lys Val Phe Thr Thr Gly Phe Ser Arg Met Ser Glu Arg Gln Leu Ala
                165                 170                 175
```

Leu Trp Asp Pro Glu Asn Leu Glu Glu Pro Met Ala Leu Gln Glu Leu
180 185 190

Asp Ser Ser Asn Gly Ala Leu Leu Pro Phe Tyr Asp Pro Asp Thr Ser
195 200 205

Val Val Tyr Val Cys Gly Lys Gly Asp Ser Ser Ile Arg Tyr Phe Glu
210 215 220

Ile Thr Glu Glu Pro Pro Tyr Ile His Phe Leu Asn Thr Phe Thr Ser
225 230 235 240

Lys Glu Pro Gln Arg Gly Met Gly Ser Met Pro Lys Arg Gly Leu Glu
245 250 255

Val Ser Lys Cys Glu Ile Ala Arg Phe Tyr Lys Leu His Glu Arg Lys
260 265 270

Cys Glu Pro Ile Val Met Thr Val Pro Arg Lys Ser Asp Leu Phe Gln
275 280 285

Asp Asp Leu Tyr Pro Asp Thr Ala Gly Pro Glu Ala Ala Leu Glu Ala
290 295 300

Glu Glu Trp Val Ser Gly Arg Asp Ala Asp Pro Ile Leu Ile Ser Leu
305 310 315 320

Arg Glu Ala Tyr Val Pro Ser Lys Gln Arg Asp Leu Lys Ile Ser Arg
325 330 335

Arg Asn Val Leu Ser Asp Ser Arg Pro Ala Met Ala Pro Gly Ser Ser
340 345 350

His Leu Gly Ala Pro Ala Ser Thr Thr Thr Ala Ala Asp Ala Thr Pro
355 360 365

Ser Gly Ser Leu Ala Arg Ala Gly Glu Ala Gly Lys Leu Glu Glu Val
370 375 380

Met Gln Glu Leu Arg Ala Leu Arg Ala Leu Val Lys Glu Gln Gly Asp
385 390 395 400

Arg Ile Cys Arg Leu Glu Glu Gln Leu Gly Arg Met Glu Asn Gly Asp
405 410 415

Ala

<210> 719

<211> 290
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (74)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (131)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 719
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Glu Leu Ser Ala Ser Ala Xaa Asp Asp Gly Asn Phe Ser Leu Leu Ile
  1               5                  10                  15

Arg Ala Val Glu Glu Thr Asp Ala Gly Leu Tyr Thr Cys Asn Leu His
             20                  25                  30

His His Tyr Cys His Leu Tyr Glu Ser Leu Ala Val Arg Leu Glu Val
         35                  40                  45

Thr Asp Gly Pro Pro Ala Pro Pro Pro Thr Gly Thr Ala Arg Arg Arg
     50                  55                  60

Cys Trp Arg Trp Arg Ala Ala Pro Ala Xaa Leu Thr Cys Val Asn Arg
 65                  70                  75                  80

Gly His Val Trp Thr Asp Arg His Val Glu Glu Ala Gln Gln Val Val
                 85                  90                  95

His Trp Asp Arg Gln Pro Pro Gly Val Pro His Asp Arg Ala Asp Arg
            100                 105                 110

Leu Leu Asp Leu Tyr Ala Ser Ala Ser Ala Ala Leu Arg Ala Pro Phe
        115                 120                 125

Ser Ala Xaa Arg Val Ala Val Gly Ala Asp Ala Phe Lys Arg Gly Asp
    130                 135                 140

Phe Ser Leu Arg Ile Glu Pro Leu Glu Val Ala Asp Glu Gly Thr Tyr
145                 150                 155                 160

Ser Cys His Leu His His His Tyr Trp Arg Ala Ala Thr Thr Ser Ser
```

165 170 175

Met Ser Ser Ser Pro Arg Ala Glu Pro Thr Ser Ser Ser Ser Trp Ala
180 185 190

Thr Cys Trp Pro Arg Cys Cys Ser Ser Ser Cys Tyr Trp Ser Leu Ser
195 200 205

Ser Trp Pro Pro Ala Gly Arg Gly Gly Tyr Glu Tyr Ser Asp Gln Lys
210 215 220

Ser Gly Lys Ser Lys Gly Lys Asp Val Asn Leu Ala Glu Phe Ala Val
225 230 235 240

Ala Ala Gly Asp Gln Met Leu Tyr Arg Ser Glu Asp Ile Gln Leu Asp
245 250 255

Tyr Lys Asn Asn Ile Leu Lys Glu Arg Ala Glu Leu Ala His Ser Pro
260 265 270

Leu Pro Ala Lys Tyr Ile Asp Leu Asp Lys Gly Phe Arg Lys Glu Asn
275 280 285

Cys Lys
290

<210> 720
<211> 459
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (50)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 720
Asp Ala His Pro Lys Pro Cys Cys Glu Thr Ser Ala Ala Ala Cys Arg
1 5 10 15

Leu Val Glu Arg Ile Leu Thr Ser Trp Glu Glu Asn Asp Arg Val Gln
20 25 30

Cys Ala Gly Gly Pro Arg Lys Gly Tyr Met Gly His Leu Thr Arg Val
35 40 45

Ala Xaa Ala Leu Val Gln Asn Thr Glu Lys Gly Pro Asn Ala Glu Gln
50 55 60

```
Leu Arg Gln Leu Leu Lys Glu Leu Pro Ser Glu Gln Gln Glu Gln Trp
 65                  70                  75                  80

Glu Ala Phe Val Ser Gly Pro Leu Ala Glu Thr Asn Lys Lys Asn Met
                 85                  90                  95

Val Asp Leu Val Asn Thr His His Leu His Ser Ser Ser Asp Asp Glu
            100                 105                 110

Asp Asp Arg Leu Lys Glu Phe Asn Phe Pro Glu Glu Ala Val Leu Gln
        115                 120                 125

Gln Ala Phe Met Asp Phe Gln Met Gln Arg Met Thr Ser Ala Phe Ile
    130                 135                 140

Asp His Phe Gly Phe Asn Asp Glu Glu Phe Gly Glu Gln Glu Glu Ser
145                 150                 155                 160

Val Asn Ala Pro Phe Asp Lys Thr Ala Asn Ile Thr Phe Ser Leu Asn
                165                 170                 175

Ala Asp Asp Glu Asn Pro Asn Ala Asn Leu Leu Glu Ile Cys Tyr Lys
            180                 185                 190

Asp Arg Ile Gln Gln Phe Asp Asp Asp Glu Glu Glu Glu Asp Glu Glu
        195                 200                 205

Glu Ala Gln Gly Ser Gly Glu Ser Asp Gly Glu Asp Gly Ala Trp Gln
    210                 215                 220

Gly Ser Gln Leu Ala Arg Gly Ala Arg Leu Gly Gln Pro Pro Gly Val
225                 230                 235                 240

Arg Ser Gly Gly Ser Thr Asp Ser Glu Asp Glu Glu Glu Glu Asp Glu
                245                 250                 255

Glu Glu Glu Glu Asp Glu Glu Gly Ile Gly Cys Ala Ala Arg Gly Gly
            260                 265                 270

Ala Thr Pro Leu Ser Tyr Pro Ser Pro Gly Pro Gln Pro Pro Gly Pro
        275                 280                 285

Ser Trp Thr Ala Thr Phe Asp Pro Val Pro Thr Asp Ala Pro Thr Ser
    290                 295                 300

Pro Arg Val Ser Gly Glu Glu Glu Leu His Thr Gly Pro Pro Ala Pro
305                 310                 315                 320

Gln Gly Pro Leu Ser Val Pro Gln Gly Leu Pro Thr Gln Ser Leu Ala
                325                 330                 335
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Ser Pro Pro Ala Arg Asp Ala Leu Gln Leu Arg Ser Gln Asp Pro Thr
            340                 345                 350

Pro Pro Ser Ala Pro Gln Glu Ala Thr Glu Gly Ser Lys Val Thr Glu
        355                 360                 365

Pro Ser Ala Pro Cys Gln Ala Leu Val Ser Ile Gly Asp Leu Gln Ala
    370                 375                 380

Thr Phe His Gly Ile Arg Ser Ala Pro Ser Ser Ser Asp Ser Ala Thr
385                 390                 395                 400

Arg Asp Pro Ser Thr Ser Val Pro Ala Ser Gly Ala His Gln Pro Pro
                405                 410                 415

Gln Thr Thr Glu Gly Glu Lys Ser Pro Glu Pro Leu Gly Leu Pro Gln
            420                 425                 430

Ser Gln Ser Ala Gln Ala Leu Thr Pro Pro Pro Ile Pro Asn Gly Ser
        435                 440                 445

Ala Pro Glu Gly Pro Ala Ser Pro Gly Ser Gln
    450                 455
```

<210> 721
<211> 523
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (194)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (327)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 721

```
Leu Gln Arg Leu Lys Leu Ile Lys Pro Leu Leu Xaa Phe Glu Ser Leu
  1               5                  10                  15

Glu Glu Cys Tyr Met Ala Lys Ile Leu Val Ala Glu Gly Thr Arg Asp
             20                  25                  30

Val Pro Ile Gly Ala Ile Ile Cys Ile Thr Val Gly Lys Pro Glu Asp
         35                  40                  45

Ile Glu Ala Phe Lys Asn Tyr Thr Leu Asp Ser Ser Ala Ala Pro Thr
     50                  55                  60

Pro Gln Ala Ala Pro Ala Pro Thr Pro Ala Ala Thr Ala Ser Pro Pro
 65                  70                  75                  80

Thr Pro Ser Ala Gln Ala Pro Gly Ser Ser Tyr Pro Pro His Met Gln
                 85                  90                  95

Val Leu Leu Pro Ala Leu Ser Pro Thr Met Thr Met Gly Thr Val Gln
            100                 105                 110

Arg Trp Xaa Lys Lys Val Gly Glu Lys Leu Ser Glu Gly Asp Leu Leu
        115                 120                 125

Ala Glu Ile Glu Thr Asp Lys Ala Thr Ile Gly Phe Glu Val Gln Glu
    130                 135                 140

Glu Gly Tyr Leu Ala Lys Ile Leu Val Pro Glu Gly Thr Arg Asp Val
145                 150                 155                 160

Pro Leu Gly Thr Pro Leu Cys Ile Ile Val Glu Lys Glu Ala Asp Ile
                165                 170                 175

Ser Ala Phe Ala Asp Tyr Arg Pro Thr Glu Val Thr Asp Leu Lys Pro
            180                 185                 190

Gln Xaa Pro Pro Pro Thr Pro Pro Pro Val Ala Ala Val Pro Pro Thr
        195                 200                 205

Pro Gln Pro Leu Ala Pro Thr Pro Ser Ala Pro Cys Pro Ala Thr Pro
    210                 215                 220

Ala Gly Pro Lys Gly Arg Val Phe Val Ser Pro Leu Ala Lys Lys Leu
225                 230                 235                 240

Ala Val Glu Lys Gly Ile Asp Leu Thr Gln Val Lys Gly Thr Gly Pro
                245                 250                 255

Asp Gly Arg Ile Thr Lys Lys Asp Ile Asp Ser Phe Val Pro Ser Lys
            260                 265                 270
```

```
Val Ala Pro Ala Pro Ala Ala Val Val Pro Pro Thr Gly Pro Gly Met
        275                 280                 285

Ala Pro Val Pro Thr Gly Val Phe Thr Asp Ile Pro Ile Ser Asn Ile
    290                 295                 300

Arg Arg Val Ile Ala Gln Arg Leu Met Gln Ser Lys Gln Thr Ile Pro
305                 310                 315                 320

His Tyr Tyr Leu Ser Ile Xaa Val Asn Met Gly Glu Val Leu Leu Val
                325                 330                 335

Arg Lys Glu Leu Asn Lys Ile Leu Glu Gly Arg Ser Lys Ile Ser Val
            340                 345                 350

Asn Asp Phe Ile Ile Lys Ala Ser Ala Leu Ala Cys Leu Lys Val Pro
        355                 360                 365

Glu Ala Asn Ser Ser Trp Met Asp Thr Val Ile Arg Gln Asn His Val
    370                 375                 380

Val Asp Val Ser Val Ala Val Ser Thr Pro Ala Gly Leu Ile Thr Pro
385                 390                 395                 400

Ile Val Phe Asn Ala His Ile Lys Gly Val Glu Thr Ile Ala Asn Asp
                405                 410                 415

Val Val Ser Leu Ala Thr Lys Ala Arg Glu Gly Lys Leu Gln Pro His
            420                 425                 430

Glu Phe Gln Gly Gly Thr Phe Thr Ile Ser Asn Leu Gly Met Phe Gly
        435                 440                 445

Ile Lys Asn Phe Ser Ala Ile Ile Asn Pro Pro Gln Ala Cys Ile Leu
    450                 455                 460

Ala Ile Gly Ala Ser Glu Asp Lys Leu Val Pro Ala Asp Asn Glu Lys
465                 470                 475                 480

Gly Phe Asp Val Ala Ser Met Met Ser Val Thr Leu Ser Cys Asp His
                485                 490                 495

Arg Val Val Asp Gly Ala Val Gly Ala Gln Trp Leu Ala Glu Phe Arg
            500                 505                 510

Lys Tyr Leu Glu Lys Pro Ile Thr Met Leu Leu
        515                 520
```

<210> 722
<211> 111
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 722
Ser Ser Arg Ser Arg Ala Ala Asp Glu Xaa Ala Leu Cys Leu Gln Cys
1 5 10 15

Asp Met Asn Asp Cys Tyr Ser Arg Leu Arg Arg Leu Val Pro Thr Ile
20 25 30

Pro Pro Asn Lys Lys Val Ser Lys Val Glu Ile Leu Gln His Val Ile
35 40 45

Asp Tyr Ile Leu Asp Leu Gln Leu Ala Leu Glu Thr His Pro Ala Leu
50 55 60

Leu Arg Gln Pro Pro Pro Pro Ala Pro Pro His His Pro Ala Gly Thr
65 70 75 80

Cys Pro Ala Ala Pro Pro Arg Thr Pro Leu Thr Ala Leu Asn Thr Asp
85 90 95

Pro Ala Gly Ala Val Asn Lys Gln Gly Asp Ser Ile Leu Cys Arg
100 105 110

<210> 723
<211> 190
<212> PRT
<213> Homo sapiens

<400> 723
Ser Gly Gly Gly Gly Gly Arg Met Ile Lys Leu Phe Ser Leu Lys Gln
1 5 10 15

Gln Lys Lys Glu Glu Glu Ser Ala Gly Gly Thr Lys Gly Ser Ser Lys
20 25 30

Lys Ala Ser Ala Ala Gln Leu Arg Ile Gln Lys Asp Ile Asn Glu Leu
35 40 45

Asn Leu Pro Lys Thr Cys Asp Ile Ser Phe Ser Asp Pro Asp Asp Leu
50 55 60

Leu Asn Phe Lys Leu Val Ile Cys Pro Asp Glu Gly Phe Tyr Lys Ser
65 70 75 80

Gly Lys Phe Val Phe Ser Phe Lys Val Gly Gln Gly Tyr Pro His Asp
85 90 95

Pro Pro Lys Val Lys Cys Glu Thr Met Val Tyr His Pro Asn Ile Asp
100 105 110

Leu Glu Gly Asn Val Cys Leu Asn Ile Leu Arg Glu Asp Trp Lys Pro
115 120 125

Val Leu Thr Ile Asn Ser Ile Ile Tyr Gly Leu Gln Tyr Leu Phe Leu
130 135 140

Glu Pro Asn Pro Glu Asp Pro Leu Asn Lys Glu Ala Ala Glu Val Leu
145 150 155 160

Gln Asn Asn Arg Arg Leu Phe Glu Gln Asn Val Gln Arg Ser Met Arg
165 170 175

Gly Gly Tyr Ile Gly Ser Thr Tyr Phe Glu Arg Cys Leu Lys
180 185 190

<210> 724
<211> 524
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (247)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (417)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (440)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (443)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 724

```
Arg Arg Arg Arg Ala Asp Arg Ala Thr Pro Arg Glu Val Leu Glu Thr
1               5                   10                  15

Pro Gly Ala Ala Ser Val Gln Thr Leu Pro Ser Val Thr Met Lys Leu
            20                  25                  30

Trp Val Ser Ala Leu Leu Met Ala Trp Phe Gly Val Leu Ser Cys Val
        35                  40                  45

Gln Ala Glu Phe Phe Thr Ser Ile Gly His Met Thr Asp Leu Ile Tyr
    50                  55                  60

Ala Glu Lys Glu Leu Val Gln Ser Leu Lys Glu Tyr Ile Leu Val Glu
65                  70                  75                  80

Glu Ala Lys Leu Ser Lys Ile Lys Ser Trp Ala Asn Lys Met Glu Ala
                85                  90                  95

Leu Thr Ser Lys Ser Ala Ala Asp Ala Glu Gly Tyr Leu Ala His Pro
            100                 105                 110

Val Asn Ala Tyr Lys Leu Val Lys Arg Leu Asn Thr Asp Trp Pro Ala
        115                 120                 125

Leu Glu Asp Leu Val Leu Gln Asp Ser Ala Ala Gly Phe Ile Ala Asn
    130                 135                 140

Leu Ser Val Gln Arg Gln Phe Phe Pro Thr Asp Glu Asp Glu Ile Gly
145                 150                 155                 160

Ala Ala Lys Ala Leu Met Arg Leu Gln Asp Thr Tyr Arg Leu Asp Pro
                165                 170                 175

Gly Thr Ile Ser Arg Gly Glu Leu Pro Gly Thr Lys Tyr Gln Ala Met
            180                 185                 190

Leu Ser Val Asp Asp Cys Phe Gly Met Gly Arg Ser Ala Tyr Asn Glu
        195                 200                 205

Gly Asp Tyr Tyr His Thr Val Leu Trp Met Glu Gln Val Leu Lys Gln
    210                 215                 220

Leu Asp Ala Gly Glu Glu Ala Thr Thr Thr Lys Ser Gln Val Leu Asp
225                 230                 235                 240

Tyr Leu Ser Tyr Ala Val Xaa Gln Leu Gly Asp Leu His Arg Ala Leu
                245                 250                 255

Glu Leu Thr Arg Arg Leu Leu Ser Leu Asp Pro Ser His Glu Arg Ala
```

```
            260                 265                 270

Gly Gly Asn Leu Arg Tyr Phe Glu Gln Leu Leu Glu Glu Glu Arg Glu
        275                 280                 285

Lys Thr Leu Thr Asn Gln Thr Glu Ala Glu Leu Ala Thr Pro Glu Gly
    290                 295                 300

Ile Tyr Glu Arg Pro Val Asp Tyr Leu Pro Glu Arg Asp Val Tyr Glu
305                 310                 315                 320

Ser Leu Cys Arg Gly Glu Gly Val Lys Leu Thr Pro Arg Arg Gln Lys
                325                 330                 335

Arg Leu Phe Cys Arg Tyr His His Gly Asn Arg Ala Pro Gln Leu Leu
            340                 345                 350

Ile Ala Pro Phe Lys Glu Glu Asp Glu Trp Asp Ser Pro His Ile Val
        355                 360                 365

Arg Tyr Tyr Asp Val Met Ser Asp Glu Glu Ile Glu Arg Ile Lys Glu
    370                 375                 380

Ile Ala Lys Pro Lys Leu Ala Arg Ala Thr Val Arg Asp Pro Lys Thr
385                 390                 395                 400

Gly Val Leu Thr Val Ala Ser Tyr Arg Val Ser Lys Ser Ser Trp Leu
                405                 410                 415

Xaa Glu Asp Asp Asp Pro Val Val Ala Arg Val Asn Arg Arg Met Gln
            420                 425                 430

His Ile Thr Gly Leu Thr Val Xaa Thr Ala Xaa Leu Leu Gln Val Ala
        435                 440                 445

Asn Tyr Gly Val Gly Gly Gln Tyr Glu Pro His Phe Asp Phe Ser Arg
    450                 455                 460

Asn Asp Glu Arg Asp Thr Phe Lys His Leu Gly Thr Gly Asn Arg Val
465                 470                 475                 480

Ala Thr Phe Leu Asn Tyr Met Ser Asp Val Glu Ala Gly Gly Ala Thr
                485                 490                 495

Val Phe Pro Asp Leu Gly Ala Ala Ile Trp Pro Lys Lys Gly Thr Ala
            500                 505                 510

Val Phe Trp Tyr Asn Leu Leu Arg Ser Gly Arg Arg
        515                 520
```

<210> 725
<211> 92
<212> PRT
<213> Homo sapiens

<400> 725
Leu Lys Met Thr Ser Leu Phe Ala Gln Glu Ile Arg Leu Ser Lys Arg
1 5 10 15

His Glu Glu Ile Val Ser Gln Arg Leu Met Leu Leu Gln Gln Met Glu
20 25 30

Asn Lys Leu Gly Asp Gln His Thr Glu Lys Ala Ser Gln Leu Gln Thr
35 40 45

Val Glu Thr Ala Phe Lys Arg Asn Leu Ser Leu Leu Lys Asp Ile Glu
50 55 60

Ala Ala Glu Lys Ser Leu Gln Thr Arg Ile His Pro Leu Pro Arg Pro
65 70 75 80

Glu Val Val Ser Leu Glu Thr Arg Tyr Trp Ala Ser
85 90

<210> 726
<211> 690
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (108)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (123)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (383)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (688)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (690)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 726
Val Ser Arg Ser Pro Arg Val Pro Leu Pro Pro Arg Ser Phe Ser Arg
1 5 10 15

Met Ala Gly Asp Ser Thr Ala Thr Ser Arg Arg Leu Gly Ala Ala Pro
20 25 30

Asp Arg Ala Ala Pro His Ile Leu Pro Ala Gly Ala His Arg Ala Ala
35 40 45

Thr Ala Pro Gly Leu Gly Gly Gly Pro Glu Pro Leu Gly Arg Ala Leu
50 55 60

Ala Gly Gly Leu Arg Gly Pro Gln Gly Asn Gly Trp Leu Gln Glu Arg
65 70 75 80

Lys Arg Arg Cys Pro Gly Leu Ala Gly Cys Phe Glu Ala Ile Ser Cys
85 90 95

Gly Thr Gly Leu Gly Leu Pro Gly Leu Ala Leu Xaa Arg Glu Leu Ile
100 105 110

Ser Trp Gly Ala Pro Gly Ser Ala Asp Ser Xaa Arg Leu Leu His Trp
115 120 125

Gly Ser His Pro Thr Ala Phe Val Val Ser Tyr Ala Ala Ala Leu Pro
130 135 140

Ala Ala Ala Leu Trp His Lys Leu Gly Ser Leu Trp Val Pro Gly Gly
145 150 155 160

Gln Gly Gly Ser Gly Asn Pro Val Arg Arg Leu Leu Gly Cys Leu Gly
165 170 175

Ser Glu Thr Arg Arg Leu Ser Leu Phe Leu Val Leu Val Val Leu Ser
180 185 190

Ser Leu Gly Glu Met Ala Ile Pro Phe Phe Thr Gly Arg Leu Thr Asp
195 200 205

Trp Ile Leu Gln Asp Gly Ser Ala Asp Thr Phe Thr Arg Asn Leu Thr
210 215 220

Leu Met Ser Ile Leu Thr Ile Ala Ser Ala Val Leu Glu Phe Val Gly
225 230 235 240

Asp Gly Ile Tyr Asn Asn Thr Met Gly His Val His Ser His Leu Gln
245 250 255

Gly Glu Val Phe Gly Ala Val Leu Arg Gln Glu Thr Glu Phe Phe Gln
260 265 270

Gln Asn Gln Thr Gly Asn Ile Met Ser Arg Val Thr Glu Asp Thr Ser
275 280 285

Thr Leu Ser Asp Ser Leu Ser Glu Asn Leu Ser Leu Phe Leu Trp Tyr
290 295 300

Leu Val Arg Gly Leu Cys Leu Leu Gly Ile Met Leu Trp Gly Ser Val
305 310 315 320

Ser Leu Thr Met Val Thr Leu Ile Thr Leu Pro Leu Leu Phe Leu Leu
325 330 335

Pro Lys Lys Val Gly Lys Trp Tyr Gln Leu Leu Glu Val Gln Val Arg
340 345 350

Glu Ser Leu Ala Lys Ser Ser Gln Val Ala Ile Glu Ala Leu Ser Ala
355 360 365

Met Pro Thr Val Arg Ser Phe Ala Asn Glu Glu Gly Glu Ala Xaa Lys
370 375 380

Phe Arg Glu Lys Leu Gln Glu Ile Lys Thr Leu Asn Gln Lys Glu Ala
385 390 395 400

Val Ala Tyr Ala Val Asn Ser Trp Thr Thr Ser Ile Ser Gly Met Leu
405 410 415

Leu Lys Val Gly Ile Leu Tyr Ile Gly Gly Gln Leu Val Thr Ser Gly
420 425 430

Ala Val Ser Ser Gly Asn Leu Val Thr Phe Val Leu Tyr Gln Met Gln
435 440 445

Phe Thr Gln Ala Val Glu Val Leu Leu Ser Ile Tyr Pro Arg Val Gln
450 455 460

Lys Ala Val Gly Ser Ser Glu Lys Ile Phe Glu Tyr Leu Asp Arg Thr
465 470 475 480

Pro Arg Cys Pro Pro Ser Gly Leu Leu Thr Pro Leu His Leu Glu Gly
485 490 495

Leu Val Gln Phe Gln Asp Val Ser Phe Ala Tyr Pro Asn Arg Pro Asp
500 505 510

```
Val Leu Val Leu Gln Gly Leu Thr Phe Thr Leu Arg Pro Gly Glu Val
        515                 520                 525

Thr Ala Leu Val Gly Pro Asn Gly Ser Gly Lys Ser Thr Val Ala Ala
    530                 535                 540

Leu Leu Gln Asn Leu Tyr Gln Pro Thr Gly Gly Gln Leu Leu Leu Asp
545                 550                 555                 560

Gly Lys Pro Leu Pro Gln Tyr Glu His Arg Tyr Leu His Arg Gln Val
                565                 570                 575

Ala Ala Val Gly Gln Glu Pro Gln Val Phe Gly Arg Ser Leu Gln Glu
            580                 585                 590

Asn Ile Ala Tyr Gly Leu Thr Gln Lys Pro Thr Met Glu Glu Ile Thr
        595                 600                 605

Ala Ala Ala Val Lys Ser Gly Ala His Ser Phe Ile Ser Gly Leu Pro
    610                 615                 620

Gln Gly Tyr Asp Thr Glu Val Asp Glu Ala Gly Ser Gln Leu Ser Gly
625                 630                 635                 640

Gly Gln Arg Gln Ala Val Ala Leu Ala Arg Ala Leu Ile Arg Lys Pro
                645                 650                 655

Cys Val Leu Ile Leu Asp Asp Ala Thr Ser Ala Leu Asp Ala Asn Ser
            660                 665                 670

Gln Leu Gln Val Glu Gln Leu Leu Tyr Glu Ser Pro Glu Arg Tyr Xaa
        675                 680                 685

Arg Xaa
    690
```

<210> 727
<211> 82
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (73)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 727
Thr Pro Pro Leu Val Ser Ser Val Ala Ala Leu Asp Ser His Arg Ser
1 5 10 15

Thr Asn Pro Ile Val Asn Ser Ala Cys Lys Gly Ser Arg Leu Cys Ala
20 25 30

Pro Tyr Glu Asn Leu Met Pro Asp Asp Leu Arg Xaa Asn Ser Phe Ile
35 40 45

Leu Lys Pro Pro Phe Thr Leu Gln Ser Val Glu Lys Leu Ser Ser Thr
50 55 60

Lys Leu Val Pro Gly Ala Lys Asn Xaa Gly Asp Arg Cys Ser Arg Glu
65 70 75 80

Arg Ser

<210> 728
<211> 600
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (11)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (479)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (550)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (588)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (590)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 728
Ser Arg Val Lys Pro Arg Val Arg Gly Thr Xaa Val Arg Thr Pro Gly
1 5 10 15

Ser Arg Arg Gly Arg His Gly Ala Val Pro Gly Asp Trp Glu Ala Ala
20 25 30

Ala Gln Ala Arg Gly Ala Gly Gln Arg Leu Pro Thr Pro Ser Glu Ile
35 40 45

Leu Ser Asn Ala Gly Leu Arg Phe Glu Val Val Pro Ser Lys Phe Lys
50 55 60

Glu Lys Leu Asp Lys Ala Ser Phe Ala Thr Pro Tyr Gly Tyr Ala Met
65 70 75 80

Glu Thr Ala Lys Gln Lys Ala Leu Glu Val Ala Asn Arg Leu Tyr Gln
85 90 95

Lys Asp Leu Arg Ala Pro Asp Val Val Ile Gly Ala Asp Thr Ile Val
100 105 110

Thr Val Gly Gly Leu Ile Leu Glu Lys Pro Val Asp Lys Gln Asp Ala
115 120 125

Tyr Arg Met Leu Ser Arg Leu Ser Gly Arg Glu His Ser Val Phe Thr
130 135 140

Gly Val Ala Ile Val His Cys Ser Ser Lys Asp His Gln Leu Asp Thr
145 150 155 160

Arg Val Ser Glu Phe Tyr Glu Glu Thr Lys Val Lys Phe Ser Glu Leu
165 170 175

Ser Glu Glu Leu Leu Trp Glu Tyr Val His Ser Gly Glu Pro Met Asp
180 185 190

Lys Ala Gly Gly Tyr Gly Ile Gln Ala Leu Gly Gly Met Leu Val Glu
195 200 205

Ser Val His Gly Asp Phe Leu Asn Val Val Gly Phe Pro Leu Asn His
210 215 220

Phe Cys Lys Gln Leu Val Lys Leu Tyr Tyr Pro Pro Arg Pro Glu Asp
225 230 235 240

Leu Arg Arg Ser Val Lys His Asp Ser Ile Pro Ala Ala Asp Thr Phe
245 250 255

```
Glu Asp Leu Ser Asp Val Glu Gly Gly Gly Ser Glu Pro Thr Gln Arg
            260                 265                 270

Asp Ala Gly Ser Arg Asp Glu Lys Ala Glu Ala Gly Glu Ala Gly Gln
        275                 280                 285

Ala Thr Ala Glu Ala Glu Cys His Arg Thr Arg Glu Thr Leu Pro Pro
    290                 295                 300

Phe Pro Thr Arg Leu Leu Glu Leu Ile Glu Gly Phe Met Leu Ser Lys
305                 310                 315                 320

Gly Leu Leu Thr Ala Cys Lys Leu Lys Val Phe Asp Leu Leu Lys Asp
                325                 330                 335

Glu Ala Pro Gln Lys Ala Ala Asp Ile Ala Ser Lys Val Asp Ala Ser
            340                 345                 350

Ala Cys Gly Met Glu Arg Leu Leu Asp Ile Cys Ala Ala Met Gly Leu
        355                 360                 365

Leu Glu Lys Thr Glu Gln Gly Tyr Ser Asn Thr Glu Thr Ala Asn Val
    370                 375                 380

Tyr Leu Ala Ser Asp Gly Glu Tyr Ser Leu His Gly Phe Ile Met His
385                 390                 395                 400

Asn Asn Asp Leu Thr Trp Asn Leu Phe Thr Tyr Leu Glu Phe Ala Ile
                405                 410                 415

Arg Glu Gly Thr Asn Gln His His Arg Ala Leu Gly Lys Lys Ala Glu
            420                 425                 430

Asp Leu Phe Gln Asp Ala Tyr Tyr Gln Ser Pro Glu Thr Arg Leu Arg
        435                 440                 445

Phe Met Arg Ala Met His Gly Met Thr Lys Leu Thr Ala Cys Gln Val
    450                 455                 460

Ala Thr Ala Phe Asn Leu Ser Arg Phe Ser Ser Ala Cys Asp Xaa Gly
465                 470                 475                 480

Gly Cys Thr Gly Ala Leu Ala Arg Glu Leu Ala Arg Glu Tyr Pro Arg
                485                 490                 495

Met Gln Val Thr Val Phe Asp Leu Pro Asp Ile Ile Glu Leu Ala Ala
            500                 505                 510

His Phe Gln Pro Pro Gly Pro Gln Gln Cys Arg Ser Thr Ser Gln Gln
        515                 520                 525
```

Val Thr Phe Ser Gly Thr Pro Ser Pro Ala Leu Ser Cys Thr Ser Cys
530 535 540

Ala Gly Ser Cys Met Xaa Gly Gln Thr Thr Lys Ser Thr Ser Tyr Ser
545 550 555 560

Ala Gly Ser Pro Arg Ala Ala Ser Gln Gly Pro Ala Cys Cys Trp Trp
565 570 575

Arg Arg Ser Trp Met Arg Arg Arg Gly Trp Arg Xaa Arg Xaa Asp Ala
580 585 590

Val Thr Glu His Ala Gly Ala Asp
595 600

<210> 729
<211> 535
<212> PRT
<213> Homo sapiens

<400> 729
Gly Arg Ser Ser Phe Thr Ser Leu Val Val Gly Val Phe Val Val Tyr
1 5 10 15

Val Val His Thr Cys Trp Val Met Tyr Gly Ile Val Tyr Thr Arg Pro
20 25 30

Cys Ser Gly Asp Ala Asn Cys Ile Gln Pro Tyr Leu Ala Arg Arg Pro
35 40 45

Lys Leu Gln Leu Ser Val Tyr Thr Thr Thr Arg Ser His Leu Gly Ala
50 55 60

Glu Asn Asn Ile Asp Leu Val Leu Asn Val Glu Asp Phe Asp Val Glu
65 70 75 80

Ser Lys Phe Glu Arg Thr Val Asn Val Ser Val Pro Lys Lys Thr Arg
85 90 95

Asn Asn Gly Thr Leu Tyr Ala Tyr Ile Phe Leu His His Ala Gly Val
100 105 110

Leu Pro Trp His Asp Gly Lys Gln Val His Leu Val Ser Pro Leu Thr
115 120 125

Thr Tyr Met Val Pro Lys Pro Glu Glu Ile Asn Leu Leu Thr Gly Glu
130 135 140

```
Ser Asp Thr Gln Gln Ile Glu Ala Glu Lys Lys Pro Thr Ser Ala Leu
145                 150                 155                 160

Asp Glu Pro Val Ser His Trp Arg Pro Arg Leu Ala Leu Asn Val Met
                165                 170                 175

Ala Asp Asn Phe Val Phe Asp Gly Ser Ser Leu Pro Ala Asp Val His
            180                 185                 190

Arg Tyr Met Lys Met Ile Gln Leu Gly Lys Thr Val His Tyr Leu Pro
        195                 200                 205

Ile Leu Phe Ile Asp Gln Leu Ser Asn Arg Val Lys Asp Leu Met Val
    210                 215                 220

Ile Asn Arg Ser Thr Thr Glu Leu Pro Leu Thr Val Ser Tyr Asp Lys
225                 230                 235                 240

Val Ser Leu Gly Arg Leu Arg Phe Trp Ile His Met Gln Asp Ala Val
                245                 250                 255

Tyr Ser Leu Gln Gln Phe Gly Phe Ser Glu Lys Asp Ala Asp Glu Val
            260                 265                 270

Lys Gly Ile Phe Val Asp Thr Asn Leu Tyr Phe Leu Ala Leu Thr Phe
        275                 280                 285

Phe Val Ala Ala Phe His Leu Leu Phe Asp Phe Leu Ala Phe Lys Asn
    290                 295                 300

Asp Ile Ser Phe Trp Lys Lys Lys Lys Ser Met Ile Gly Met Ser Thr
305                 310                 315                 320

Lys Ala Val Leu Trp Arg Cys Phe Ser Thr Val Val Ile Phe Leu Phe
                325                 330                 335

Leu Leu Asp Glu Gln Thr Ser Leu Leu Val Leu Val Pro Ala Gly Val
            340                 345                 350

Gly Ala Ala Ile Glu Leu Trp Lys Val Lys Lys Ala Leu Lys Met Thr
        355                 360                 365

Ile Phe Trp Arg Gly Leu Met Pro Glu Phe Gln Phe Gly Thr Tyr Ser
    370                 375                 380

Glu Ser Glu Arg Lys Thr Glu Glu Tyr Asp Thr Gln Ala Met Lys Tyr
385                 390                 395                 400

Leu Ser Tyr Leu Leu Tyr Pro Leu Cys Val Gly Gly Ala Val Tyr Ser
                405                 410                 415
```

Leu Leu Asn Ile Lys Tyr Lys Ser Trp Tyr Ser Trp Leu Ile Asn Ser
420 425 430

Phe Val Asn Gly Val Tyr Ala Phe Gly Phe Leu Phe Met Leu Pro Gln
435 440 445

Leu Phe Val Asn Tyr Lys Leu Lys Ser Val Ala His Leu Pro Trp Lys
450 455 460

Ala Phe Thr Tyr Lys Ala Phe Asn Thr Phe Ile Asp Asp Val Phe Ala
465 470 475 480

Phe Ile Ile Thr Met Pro Thr Ser His Arg Leu Ala Cys Phe Arg Asp
485 490 495

Asp Val Val Phe Leu Val Tyr Leu Tyr Gln Arg Trp Leu Tyr Pro Val
500 505 510

Asp Lys Arg Arg Val Asn Glu Phe Gly Glu Ser Tyr Glu Glu Lys Ala
515 520 525

Thr Arg Ala Pro His Thr Asp
530 535

<210> 730
<211> 288
<212> PRT
<213> Homo sapiens

<400> 730
Arg Pro Ala Gly Val Thr Glu Leu Gln Pro Arg Ala Pro Gly Gly Gly
1 5 10 15

Gly Met Glu Ala Ala Ala Glu Pro Gly Asn Leu Ala Gly Val Arg His
20 25 30

Ile Ile Leu Val Leu Ser Gly Lys Gly Gly Val Gly Lys Ser Thr Ile
35 40 45

Ser Thr Glu Leu Ala Leu Ala Leu Arg His Ala Gly Lys Lys Val Gly
50 55 60

Ile Leu Asp Val Asp Leu Cys Gly Pro Ser Ile Pro Arg Met Leu Gly
65 70 75 80

Ala Gln Gly Arg Ala Val His Gln Cys Asp Arg Gly Trp Ala Pro Val
85 90 95

Phe Leu Asp Arg Glu Gln Ser Ile Ser Leu Met Ser Val Gly Phe Leu

100 105 110

Leu Glu Lys Pro Asp Glu Ala Val Val Trp Arg Gly Pro Lys Lys Asn
115 120 125

Ala Leu Ile Lys Gln Phe Val Ser Asp Val Ala Trp Gly Glu Leu Asp
130 135 140

Tyr Leu Val Val Asp Thr Pro Pro Gly Thr Ser Asp Glu His Met Ala
145 150 155 160

Thr Ile Glu Ala Leu Arg Pro Tyr Gln Pro Leu Gly Ala Leu Val Val
165 170 175

Thr Thr Pro Gln Ala Val Ser Val Gly Asp Val Arg Arg Glu Leu Thr
180 185 190

Phe Cys Arg Lys Thr Gly Leu Arg Val Met Gly Ile Val Glu Asn Met
195 200 205

Ser Gly Phe Thr Cys Pro His Cys Thr Glu Cys Thr Ser Val Phe Ser
210 215 220

Arg Gly Gly Gly Glu Glu Leu Ala Gln Leu Ala Gly Val Pro Phe Leu
225 230 235 240

Gly Ser Val Pro Leu Asp Pro Ala Leu Met Arg Thr Leu Glu Glu Gly
245 250 255

His Asp Phe Ile Gln Glu Phe Pro Gly Ser Pro Ala Phe Ala Ala Leu
260 265 270

Thr Ser Ile Ala Gln Lys Ile Leu Asp Ala Thr Pro Ala Cys Leu Pro
275 280 285

<210> 731
<211> 737
<212> PRT
<213> Homo sapiens

<400> 731
Asp Gln Leu Cys Gly Pro Gln Thr Tyr Lys Glu His Leu Glu Gly Gln
1 5 10 15

Lys His Lys Lys Lys Glu Ala Ala Leu Lys Ala Ser Gln Asn Thr Ser
20 25 30

Ser Ser Asn Ser Ser Thr Arg Gly Thr Gln Asn Gln Leu Arg Cys Glu
35 40 45

Leu Cys Asp Val Ser Cys Thr Gly Ala Asp Ala Tyr Ala Ala His Ile
50 55 60

Arg Gly Ala Lys His Gln Lys Val Val Lys Leu His Thr Lys Leu Gly
65 70 75 80

Lys Pro Ile Pro Ser Thr Glu Pro Asn Val Val Ser Gln Ala Thr Ser
85 90 95

Ser Thr Ala Val Ser Ala Ser Lys Pro Thr Ala Ser Pro Ser Ser Ile
100 105 110

Ala Ala Asn Asn Cys Thr Val Asn Thr Ser Ser Ile Ala Thr Ser Ser
115 120 125

Met Lys Gly Leu Thr Thr Thr Gly Asn Ser Ser Leu Asn Ser Thr Ser
130 135 140

Asn Thr Lys Val Ser Ala Val Pro Thr Asn Met Ala Ala Lys Lys Thr
145 150 155 160

Ser Thr Pro Lys Ile Asn Phe Val Gly Gly Asn Lys Leu Gln Ser Thr
165 170 175

Gly Asn Lys Ala Glu Asp Thr Lys Gly Thr Glu Cys Val Lys Ser Thr
180 185 190

Pro Val Thr Ser Ala Val Gln Ile Pro Glu Val Lys Gln Asp Thr Val
195 200 205

Ser Glu Pro Val Thr Pro Ala Ser Leu Ala Ala Leu Gln Ser Asp Val
210 215 220

Gln Pro Val Gly His Asp Tyr Val Glu Glu Val Arg Asn Asp Glu Gly
225 230 235 240

Lys Val Ile Arg Phe His Cys Lys Leu Cys Glu Cys Ser Phe Asn Asp
245 250 255

Pro Asn Ala Lys Glu Met His Leu Lys Gly Arg Arg His Arg Leu Gln
260 265 270

Tyr Lys Lys Lys Val Asn Pro Asp Leu Gln Val Glu Val Lys Pro Ser
275 280 285

Ile Arg Ala Arg Lys Ile Gln Glu Glu Lys Met Arg Lys Gln Met Gln
290 295 300

Lys Glu Glu Tyr Trp Arg Arg Arg Glu Glu Glu Glu Arg Trp Arg Met
305 310 315 320

Glu Met Arg Arg Tyr Glu Glu Asp Met Tyr Trp Arg Arg Met Glu Glu
325 330 335

Glu Gln His His Trp Asp Asp Arg Arg Arg Met Pro Asp Gly Gly Tyr
340 345 350

Pro His Gly Pro Pro Gly Pro Leu Gly Leu Leu Gly Val Arg Pro Gly
355 360 365

Met Pro Pro Gln Pro Gln Gly Pro Ala Pro Leu Arg Arg Pro Asp Ser
370 375 380

Ser Asp Asp Arg Tyr Val Met Thr Lys His Ala Thr Ile Tyr Pro Thr
385 390 395 400

Glu Glu Glu Leu Gln Ala Val Gln Lys Ile Val Ser Ile Thr Glu Arg
405 410 415

Ala Leu Lys Leu Val Ser Asp Ser Leu Ser Glu His Glu Lys Asn Lys
420 425 430

Asn Lys Glu Gly Asp Asp Lys Lys Glu Gly Gly Lys Asp Arg Ala Leu
435 440 445

Lys Gly Val Leu Arg Val Gly Val Leu Ala Lys Gly Leu Leu Leu Arg
450 455 460

Gly Asp Arg Asn Val Asn Leu Val Leu Leu Cys Ser Glu Lys Pro Ser
465 470 475 480

Lys Thr Leu Leu Ser Arg Ile Ala Glu Asn Leu Pro Lys Gln Leu Ala
485 490 495

Val Ile Ser Pro Glu Lys Tyr Asp Ile Lys Cys Ala Val Ser Glu Ala
500 505 510

Ala Ile Ile Leu Asn Ser Cys Val Glu Pro Lys Met Gln Val Thr Ile
515 520 525

Thr Leu Thr Ser Pro Ile Ile Arg Glu Glu Asn Met Arg Glu Gly Asp
530 535 540

Val Thr Ser Gly Met Val Lys Asp Pro Pro Asp Val Leu Asp Arg Gln
545 550 555 560

Lys Cys Leu Asp Ala Leu Ala Ala Leu Arg His Ala Lys Trp Phe Gln
565 570 575

Ala Arg Ala Asn Gly Leu Gln Ser Cys Val Ile Ile Ile Arg Ile Leu
580 585 590

Arg Asp Leu Cys Gln Arg Val Pro Thr Trp Ser Asp Phe Pro Ser Trp
595 600 605

Ala Met Glu Leu Leu Val Glu Lys Ala Ile Ser Ser Ala Ser Ser Pro
610 615 620

Gln Ser Pro Gly Asp Ala Leu Arg Arg Val Phe Glu Cys Ile Ser Ser
625 630 635 640

Gly Ile Ile Leu Lys Gly Ser Pro Gly Leu Leu Asp Pro Cys Glu Lys
645 650 655

Asp Pro Phe Asp Thr Leu Ala Thr Met Thr Asp Gln Gln Arg Glu Asp
660 665 670

Ile Thr Ser Ser Ala Gln Phe Ala Leu Arg Leu Leu Ala Phe Arg Gln
675 680 685

Ile His Lys Val Leu Gly Met Asp Pro Leu Pro Gln Met Ser Gln Arg
690 695 700

Phe Asn Ile His Asn Asn Arg Lys Arg Arg Arg Asp Ser Asp Gly Val
705 710 715 720

Asp Gly Phe Glu Ala Glu Gly Lys Lys Asp Lys Lys Asp Tyr Asp Asn
725 730 735

Phe

<210> 732
<211> 106
<212> PRT
<213> Homo sapiens

<400> 732
Gly Arg Gly Leu Asn Ser Pro Lys Glu Leu Arg Pro Leu Thr Arg Ala
1 5 10 15

Ala Pro Ala Ala Ala Ala Cys Thr Gly Pro Gly Ala Ala Met Pro Lys
20 25 30

Cys Pro Lys Cys Asn Lys Glu Val Tyr Phe Ala Glu Arg Val Thr Ser
35 40 45

Leu Gly Lys Asp Trp His Arg Pro Cys Leu Lys Cys Glu Lys Cys Gly
50 55 60

Lys Thr Leu Thr Ser Gly Gly His Ala Glu His Glu Gly Lys Pro Tyr
65 70 75 80

Cys Asn His Pro Cys Tyr Ala Ala Met Phe Gly Pro Lys Gly Phe Gly
85 90 95

Arg Gly Gly Ala Glu Ser His Thr Phe Lys
100 105

<210> 733
<211> 230
<212> PRT
<213> Homo sapiens

<400> 733
Ala Ser Cys Leu Gln Ser Val Ala Ser Ala Cys Ala Ser Phe Pro Ala
1 5 10 15

Pro Ser Trp Arg Gly Thr Arg Lys Arg Asn Ala Thr Asp Arg Val Thr
20 25 30

Gln Cys Lys Tyr Lys Arg Ile Gly Cys Pro Trp His Gly Pro Phe His
35 40 45

Glu Leu Thr Val His Glu Ala Ala Cys Ala His Pro Thr Lys Thr Gly
50 55 60

Ser Glu Leu Met Glu Ile Leu Asp Gly Met Asp Gln Ser His Arg Lys
65 70 75 80

Glu Met Gln Leu Tyr Asn Ser Ile Phe Ser Leu Leu Ser Phe Glu Lys
85 90 95

Ile Gly Tyr Thr Glu Val Gln Phe Arg Pro Tyr Arg Thr Asp Asp Phe
100 105 110

Ile Thr Arg Leu Tyr Tyr Glu Thr Pro Arg Phe Thr Val Leu Asn Gln
115 120 125

Thr Trp Val Leu Lys Ala Arg Val Asn Asp Ser Glu Arg Asn Pro Asn
130 135 140

Leu Ser Cys Lys Arg Thr Leu Ser Phe Gln Leu Leu Leu Lys Ser Lys
145 150 155 160

Val Thr Ala Pro Leu Glu Cys Ser Phe Leu Leu Leu Lys Gly Pro Tyr

165 170 175

Asp Asp Val Arg Ile Ser Pro Val Ile Tyr His Phe Val Phe Thr Asn
180 185 190

Glu Ser Asn Glu Thr Asp Tyr Val Pro Leu Pro Ile Ile Asp Ser Val
195 200 205

Glu Cys Asn Lys Leu Leu Ala Ala Lys Asn Ile Asn Leu Arg Leu Phe
210 215 220

Leu Phe Gln Ile Gln Lys
225 230

<210> 734
<211> 222
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 734
Gly Arg Pro Ala Pro Pro Ala Ala Arg Ala Gly Ala His Ser Arg Gly
1 5 10 15

Ala Xaa Ala Pro Pro Ala Ala Ile Asp Met Met Phe Pro Gln Ser Arg
20 25 30

His Ser Gly Ser Ser His Leu Pro Gln Gln Leu Lys Phe Thr Thr Ser
35 40 45

Asp Ser Cys Asp Arg Ile Lys Asp Glu Phe Gln Leu Leu Gln Ala Gln
50 55 60

Tyr His Ser Leu Lys Leu Glu Cys Asp Lys Leu Ala Ser Glu Lys Ser
65 70 75 80

Glu Met Gln Arg His Tyr Val Met Tyr Tyr Glu Met Ser Tyr Gly Leu
85 90 95

Asn Ile Glu Met His Lys Gln Ala Glu Ile Val Lys Arg Leu Asn Gly
100 105 110

Ile Cys Ala Gln Val Leu Pro Tyr Leu Ser Gln Glu His Gln Gln Gln
115 120 125

Val Leu Gly Ala Ile Glu Arg Ala Lys Gln Val Thr Ala Pro Glu Leu
130 135 140

Asn Ser Ile Ile Arg Gln Gln Leu Gln Ala His Gln Leu Ser Gln Leu
145 150 155 160

Gln Ala Leu Ala Leu Pro Leu Thr Pro Leu Pro Val Gly Leu Gln Pro
165 170 175

Pro Ser Leu Pro Ala Val Ser Ala Gly Thr Gly Leu Leu Ser Leu Ser
180 185 190

Ala Leu Gly Ser Gln Ala His Leu Ser Lys Glu Asp Lys Asn Gly His
195 200 205

Asp Gly Asp Thr His Gln Glu Asp Asp Gly Glu Lys Ser Asp
210 215 220

<210> 735
<211> 248
<212> PRT
<213> Homo sapiens

<400> 735
Gly Thr Ser Asp Met Glu Leu Phe Leu Ala Gly Arg Arg Val Leu Val
1 5 10 15

Thr Gly Ala Gly Lys Gly Ile Gly Arg Gly Thr Val Gln Ala Leu His
20 25 30

Ala Thr Gly Ala Arg Val Val Ala Val Ser Arg Thr Gln Ala Asp Leu
35 40 45

Asp Ser Leu Val Arg Glu Cys Pro Gly Ile Glu Pro Val Cys Val Asp
50 55 60

Leu Gly Asp Trp Glu Ala Thr Glu Arg Ala Leu Gly Ser Val Gly Pro
65 70 75 80

Val Asp Leu Leu Val Asn Asn Ala Ala Val Ala Leu Leu Gln Pro Phe
85 90 95

Leu Glu Val Thr Lys Glu Ala Phe Asp Arg Ser Phe Glu Val Asn Leu
100 105 110

Arg Ala Val Ile Gln Val Ser Gln Ile Val Ala Arg Gly Leu Ile Ala
115 120 125

Arg Gly Val Pro Gly Ala Ile Val Asn Val Ser Ser Gln Cys Ser Gln

130 135 140

Arg Ala Val Thr Asn His Ser Val Tyr Cys Ser Thr Lys Gly Ala Leu
145 150 155 160

Asp Met Leu Thr Lys Val Met Ala Leu Glu Leu Gly Pro His Lys Ile
165 170 175

Arg Val Asn Ala Val Asn Pro Thr Val Val Met Thr Ser Met Gly Gln
180 185 190

Ala Thr Trp Ser Asp Pro His Lys Ala Lys Thr Met Leu Asn Arg Ile
195 200 205

Pro Leu Gly Lys Phe Ala Glu Val Glu His Val Val Asn Ala Ile Leu
210 215 220

Phe Leu Leu Ser Asp Arg Ser Gly Met Thr Thr Gly Ser Thr Leu Pro
225 230 235 240

Val Glu Gly Gly Phe Trp Ala Cys
245

<210> 736
<211> 216
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (61)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 736
Arg Leu Leu Phe Arg Val Arg Lys Arg Met Ile Ser Phe Ser Ala Pro
1 5 10 15

Pro Leu Met Leu Pro Phe Ser Phe Tyr Phe Phe Val Phe Pro Val Ala
20 25 30

Arg Thr Ala Arg Lys Arg Lys Pro Ser Pro Glu Pro Glu Gly Glu Val
35 40 45

Gly Pro Pro Lys Ile Asn Gly Glu Ala Gln Pro Trp Xaa Ser Thr Ser

```
    50                  55                  60

Thr Glu Gly Xaa Lys Ile Pro Met Thr Pro Thr Ser Ser Phe Val Ser
65                  70                  75                  80

Pro Pro Pro Pro Thr Ala Ser Pro His Ser Asn Arg Thr Thr Pro Pro
                85                  90                  95

Glu Ala Ala Gln Asn Gly Gln Ser Pro Met Ala Ala Leu Ile Leu Val
            100                 105                 110

Ala Asp Asn Ala Gly Gly Ser His Ala Ser Lys Asp Ala Asn Gln Val
        115                 120                 125

His Ser Thr Thr Arg Arg Asn Ser Asn Ser Pro Pro Ser Pro Ser Ser
    130                 135                 140

Met Asn Gln Arg Arg Leu Gly Pro Arg Glu Val Gly Gly Gln Gly Ala
145                 150                 155                 160

Gly Asn Thr Gly Gly Leu Glu Pro Val His Pro Ala Ser Leu Pro Asp
                165                 170                 175

Phe Ser Leu Ala Thr Ser Ala Pro Leu Cys Cys Thr Leu Cys His Glu
            180                 185                 190

Arg Leu Glu Asp Asn His Phe Val Gln Cys Arg Pro Ser Phe Asp Lys
        195                 200                 205

Phe Ser Ser Leu Leu Arg Gln Arg
    210                 215
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<210> 737
<211> 317
<212> PRT
<213> Homo sapiens

<400> 737

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Arg Pro Thr Arg Pro Glu Val Met Met Thr Lys Tyr Ser Asn Leu Ser
1               5                   10                  15

Leu Glu Ser His Asn Phe Ser Leu Thr Ala Ser Pro Leu Thr Ser Leu
            20                  25                  30

Pro Ile Pro Glu Val Met Met Thr Lys Tyr Ser Asn Leu Phe Leu Glu
        35                  40                  45

Ser His Asn Ile Ser Leu Thr Glu His Ser Ser Val Pro Val Glu Lys
    50                  55                  60
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Asn Ile Thr Leu Glu Arg Pro Ser Ala Val Glu Leu Thr Cys Gln Phe
 65                  70                  75                  80

Thr Thr Ser Gly Asp Val Asn Ser Val Asn Val Thr Trp Lys Lys Gly
                 85                  90                  95

Asp Glu Gln Leu Lys Asn Tyr His Val Ser Ala Thr Glu Gly Ile Leu
            100                 105                 110

Tyr Thr Gln Tyr Lys Phe Ser Ile Ile Asn Ser Glu Gln Leu Gly Ser
        115                 120                 125

Tyr Ser Cys Phe Phe Glu Glu Glu Lys Glu Arg Arg Gly Thr Phe Asn
    130                 135                 140

Phe Gly Val Pro Glu Val Gln Arg Lys Asn Lys Pro Leu Ile Thr Tyr
145                 150                 155                 160

Val Gly Asp Ser Val Val Leu Val Cys Lys Cys Arg His Cys Ala Pro
                165                 170                 175

Leu Asn Trp Thr Trp Tyr Ser Gly Asn Arg Ser Val Gln Val Pro Leu
            180                 185                 190

Asp Val His Met Asn Glu Lys Tyr Ala Ile Asn Gly Thr Asn Ala Asn
        195                 200                 205

Glu Thr Arg Leu Lys Ile Met Gln Leu Ser Glu Asp Asp Lys Gly Ser
    210                 215                 220

Tyr Trp Cys His Ala Met Phe Gln Leu Gly Glu Ser Gln Glu Ser Val
225                 230                 235                 240

Glu Leu Val Val Ile Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Gly
                245                 250                 255

Ile Val Val Glu Val Ile Leu Leu Val Ala Ile Ile Leu Phe Cys Glu
            260                 265                 270

Met His Thr Gln Lys Lys Lys Met His Met Asp Asp Gly Lys Glu Phe
        275                 280                 285

Glu Gln Val Glu Gln Leu Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn
    290                 295                 300

Asn Ala Pro Arg His Arg Lys Asn Glu Ala Met Ser Gln
305                 310                 315
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<210> 738
<211> 67
<212> PRT
<213> Homo sapiens

<400> 738
Ala Arg Val Ala Ser Asp Pro Phe Phe Arg His Tyr Arg Gln Leu Asn
1   5   10   15

Glu Lys Leu Val Gln Leu Ile Glu Asp Tyr Ser Leu Val Ser Phe Ile
            20   25   30

Pro Leu Asn Ile Gln Asp Lys Glu Ser Ile Gln Arg Val Leu Gln Ala
        35   40   45

Val Asp Lys Ala Asn Gly Tyr Cys Phe Gly Ala Gln Glu Gln Arg Thr
    50   55   60

Trp Lys Pro
65

<210> 739
<211> 142
<212> PRT
<213> Homo sapiens

<400> 739
Ser Gln Gln Pro Arg Ile Met Ser Lys Leu Gly Arg Ala Ala Arg Gly
1   5   10   15

Leu Arg Lys Pro Glu Val Gly Gly Val Ile Arg Ala Ile Val Arg Ala
            20   25   30

Gly Leu Ala Met Pro Gly Pro Pro Leu Gly Pro Val Leu Gly Gln Arg
        35   40   45

Gly Val Ser Ile Asn Gln Phe Cys Lys Glu Phe Asn Glu Arg Thr Lys
    50   55   60

Asp Ile Lys Glu Gly Ile Pro Leu Pro Thr Lys Ile Leu Val Lys Pro
65   70   75   80

Asp Arg Thr Phe Glu Ile Lys Ile Gly Gln Pro Thr Val Ser Tyr Phe
                85   90   95

Leu Lys Ala Ala Ala Gly Ile Glu Lys Gly Ala Arg Gln Thr Gly Lys
            100   105   110

Glu Val Ala Gly Leu Val Thr Leu Lys His Val Tyr Glu Ile Ala Arg

115 120 125

Ile Lys Ala Gln Asp Glu Ala Phe Ala Cys Arg Met Tyr Pro
130 135 140

<210> 740
<211> 485
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 740
Trp Pro Ala Val Ala Val Arg Phe Thr Ala Leu Xaa Leu Gly Phe Gly
1 5 10 15

Asp Ala Val His Val Tyr Asp Gly Pro Gly Pro Pro Glu Ser Ser Arg
20 25 30

Leu Leu Arg Ser Leu Thr His Phe Ser Asn Gly Lys Ala Val Thr Val
35 40 45

Glu Thr Leu Ser Gly Gln Ala Val Val Ser Tyr His Thr Val Ala Trp
50 55 60

Ser Asn Gly Arg Gly Phe Asn Ala Thr Tyr His Val Arg Gly Tyr Cys
65 70 75 80

Leu Pro Trp Asp Arg Pro Cys Gly Leu Gly Ser Gly Leu Gly Ala Gly
85 90 95

Glu Gly Leu Gly Glu Arg Cys Tyr Ser Glu Ala Gln Arg Cys Asp Gly
100 105 110

Ser Trp Asp Cys Ala Asp Gly Thr Asp Glu Glu Asp Cys Pro Gly Cys
115 120 125

Pro Pro Gly His Phe Pro Cys Gly Ala Ala Gly Thr Ser Gly Ala Thr
130 135 140

Ala Cys Tyr Leu Pro Ala Asp Arg Cys Asn Tyr Gln Thr Phe Cys Ala
145 150 155 160

Asp Gly Ala Asp Glu Arg Arg Cys Arg His Cys Gln Pro Gly Asn Phe
165 170 175

Arg Cys Arg Asp Glu Lys Cys Val Tyr Glu Thr Trp Val Cys Asp Gly
180 185 190

Gln Pro Asp Cys Ala Asp Gly Ser Asp Glu Trp Asp Cys Ser Tyr Val
195 200 205

Leu Pro Arg Lys Val Ile Thr Ala Ala Val Ile Gly Ser Leu Val Cys
210 215 220

Gly Leu Leu Leu Val Ile Ala Leu Gly Cys Thr Cys Lys Leu Tyr Ala
225 230 235 240

Ile Arg Thr Gln Glu Tyr Ser Ile Phe Ala Pro Leu Ser Arg Met Glu
245 250 255

Ala Glu Ile Val Gln Gln Gln Ala Pro Pro Ser Tyr Gly Gln Leu Ile
260 265 270

Ala Gln Gly Ala Ile Pro Pro Val Glu Asp Phe Pro Thr Glu Asn Pro
275 280 285

Asn Asp Asn Ser Val Leu Gly Asn Leu Arg Ser Leu Leu Gln Ile Leu
290 295 300

Arg Gln Asp Met Thr Pro Gly Gly Gly Pro Gly Ala Arg Arg Arg Gln
305 310 315 320

Arg Gly Arg Leu Met Arg Arg Leu Val Arg Arg Leu Arg Arg Trp Gly
325 330 335

Leu Leu Pro Arg Thr Asn Thr Pro Ala Arg Ala Ser Glu Ala Arg Ser
340 345 350

Gln Val Thr Pro Ser Ala Ala Pro Leu Glu Ala Leu Asp Gly Gly Thr
355 360 365

Gly Pro Ala Arg Glu Gly Gly Ala Val Gly Gly Gln Asp Gly Glu Gln
370 375 380

Ala Pro Pro Leu Pro Ile Lys Ala Pro Leu Pro Ser Ala Ser Thr Ser
385 390 395 400

Pro Ala Pro Thr Thr Val Pro Glu Ala Pro Gly Pro Leu Pro Ser Leu
405 410 415

Pro Leu Glu Pro Ser Leu Leu Ser Gly Val Val Gln Ala Leu Arg Gly
420 425 430

Arg Leu Leu Pro Ser Leu Gly Pro Pro Gly Pro Thr Arg Ser Pro Pro
435 440 445

Gly Pro His Thr Ala Val Leu Ala Leu Glu Asp Glu Asp Asp Val Leu
450 455 460

Leu Val Pro Leu Ala Glu Pro Gly Val Trp Val Ala Glu Ala Glu Asp
465 470 475 480

Glu Pro Leu Leu Thr
485

<210> 741
<211> 313
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (36)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (276)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 741
Gly Gly Ala Arg Gly Xaa Xaa Arg Xaa Val Ala Ser Phe Gln Gln Gln
1 5 10 15

His Gly Ala Gln Arg Asp Leu Lys Leu Gly Ser Arg Leu Tyr Gly Pro
20 25 30

Ser Ser Val Xaa Phe Ala Glu Asp Phe Val Arg Ser Ser Lys Gln His
35 40 45

Tyr Asn Cys Glu His Ser Lys Ile Asn Phe Arg Asp Lys Arg Ser Ala
50 55 60

Leu Gln Ser Ile Asn Glu Trp Ala Ala Gln Thr Thr Asp Gly Lys Leu
65 70 75 80

Pro Glu Val Thr Lys Asp Val Glu Arg Thr Asp Gly Ala Leu Leu Val
85 90 95

Asn Ala Met Phe Phe Lys Pro His Trp Asp Glu Lys Phe His His Lys
100 105 110

Met Val Asp Asn Arg Gly Phe Met Val Thr Arg Ser Tyr Thr Val Gly
115 120 125

Val Thr Met Met His Arg Thr Gly Leu Tyr Asn Tyr Tyr Asp Asp Glu
130 135 140

Lys Glu Lys Leu Gln Met Val Glu Met Pro Leu Ala His Lys Leu Ser
145 150 155 160

Ser Leu Leu Ile Leu Met Pro His His Val Glu Pro Leu Glu Arg Leu
165 170 175

Glu Lys Leu Leu Thr Lys Glu Gln Leu Lys Ile Trp Met Gly Lys Met
180 185 190

Gln Lys Lys Ala Val Ala Ile Ser Leu Pro Lys Gly Val Val Glu Val
195 200 205

Thr His Asp Leu Gln Lys His Leu Ala Gly Leu Gly Leu Thr Glu Ala
210 215 220

Ile Asp Lys Asn Lys Ala Asp Leu Ser Arg Met Ser Gly Lys Lys Asp
225 230 235 240

Leu Tyr Leu Ala Ser Val Phe His Ala Thr Ala Phe Glu Trp Asp Thr
245 250 255

Glu Gly Asn Pro Phe Asp Gln Asp Ile Tyr Gly Arg Glu Glu Leu Arg
260 265 270

Ser Pro Lys Xaa Phe Tyr Ala Asp His Pro Phe Ile Phe Leu Val Arg
275 280 285

Asp Thr Gln Thr Gly Ser Leu Leu Phe Ile Gly Arg Leu Val Arg Pro
290 295 300

Lys Gly Asp Lys Met Arg Asp Glu Leu
305 310

<210> 742
<211> 60
<212> PRT
<213> Homo sapiens

<400> 742
Arg Asn Ile Lys Trp Glu Lys Ala Tyr Lys Ala Phe Arg Ile Leu Ser
1 5 10 15

Val Ser Ser Phe Leu Val Phe Arg Cys Tyr Val Ile Lys His Ile Phe
20 25 30

Phe Gly Phe Pro Arg Tyr Thr Ile Tyr Leu Phe Lys Gly Lys Ser Ile
35 40 45

Lys Cys Ile Tyr Phe Ile Leu Trp Phe Cys Tyr Leu
50 55 60

<210> 743
<211> 204
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (4)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 743
Pro Arg Gly Xaa Ser Gln Val Cys Pro Cys Ser Trp Asn Pro Gly Val
1 5 10 15

Pro Glu Ala Lys Ala Pro Pro Arg Gly Ser Arg Glu Asp Leu Val Ala
20 25 30

Glu Glu Ser Pro Glu Leu Leu Asn Pro Glu Pro Arg Arg Leu Ser Pro
35 40 45

Glu Leu Arg Leu Leu Pro Tyr Met Ile Thr Leu Gly Asp Ala Val His
50 55 60

Asn Phe Ala Asp Gly Leu Ala Val Gly Ala Ala Phe Ala Ser Ser Trp
65 70 75 80

Lys Thr Gly Leu Ala Thr Ser Leu Ala Val Phe Cys His Glu Leu Pro
85 90 95

His Glu Leu Gly Asp Phe Ala Ala Leu Leu His Ala Gly Leu Ser Val
100 105 110

Arg Gln Ala Leu Leu Leu Asn Leu Ala Ser Ala Leu Thr Ala Phe Ala
115 120 125

Gly Leu Tyr Val Ala Leu Ala Val Gly Val Ser Glu Glu Ser Glu Ala
130 135 140

Trp Ile Leu Ala Val Ala Thr Gly Leu Phe Leu Tyr Val Ala Leu Cys
145 150 155 160

Asp Met Leu Pro Ala Met Leu Lys Val Arg Asp Pro Arg Pro Trp Leu
165 170 175

Leu Phe Leu Leu His Asn Val Gly Leu Leu Gly Gly Trp Thr Val Leu
180 185 190

Leu Leu Leu Ser Leu Tyr Glu Asp Asp Ile Thr Phe
195 200

<210> 744
<211> 81
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 744
Ile Thr Lys Gly Lys Xaa Val Ala Cys Ser Thr Gly Pro Glu Phe Pro
1 5 10 15

Gly Arg Pro Thr Arg Pro Thr Thr Glu Gly Tyr Gly Cys Glu Lys Thr
20 25 30

Thr Glu Gly Tyr Gly Cys Glu Lys Thr Thr Glu Gly Tyr Gly Cys Glu
35 40 45

Lys Thr Thr Glu Gly Tyr Gly Cys Glu Lys Thr Thr Glu Gly Tyr Gly
50 55 60

Cys Glu Lys Thr Thr Glu Gly Thr Ala Ala Arg Arg Arg Gln Arg Val
65 70 75 80

Arg

<210> 745
<211> 751
<212> PRT
<213> Homo sapiens

<400> 745
Leu Pro Pro Leu Gly Ser Pro Gly Pro Ala Arg Ser Ala Gly Ser Cys
1 5 10 15

Ser Val Leu Phe Ser Leu Ile Leu Gln Arg Gln Asp Pro Ala Pro Ala
20 25 30

Leu Ser Thr Ala Thr Met Gly Lys Gly Val Gly Arg Asp Lys Tyr Glu
35 40 45

Pro Ala Ala Val Ser Glu Gln Gly Asp Lys Lys Gly Lys Lys Gly Lys
50 55 60

Lys Asp Arg Asp Met Asp Glu Leu Lys Lys Glu Val Ser Met Asp Asp
65 70 75 80

His Lys Leu Ser Leu Asp Glu Leu His Arg Lys Tyr Gly Thr Asp Leu
85 90 95

Ser Arg Gly Leu Thr Ser Ala Arg Ala Ala Glu Ile Leu Ala Arg Asp
100 105 110

Gly Pro Asn Ala Leu Thr Pro Pro Pro Thr Thr Pro Glu Trp Ile Lys
115 120 125

Phe Cys Arg Gln Leu Phe Gly Gly Phe Ser Met Leu Leu Trp Ile Gly
130 135 140

Ala Ile Leu Cys Phe Leu Ala Tyr Ser Ile Gln Ala Ala Thr Glu Glu
145 150 155 160

Glu Pro Gln Asn Asp Asn Leu Tyr Leu Gly Val Val Leu Ser Ala Val
165 170 175

Val Ile Ile Thr Gly Cys Phe Ser Tyr Tyr Gln Glu Ala Lys Ser Ser
180 185 190

Lys Ile Met Glu Ser Phe Lys Asn Met Val Pro Gln Gln Ala Leu Val
195 200 205

Ile Arg Asn Gly Glu Lys Met Ser Ile Asn Ala Glu Glu Val Val Val
210 215 220

Gly Asp Leu Val Glu Val Lys Gly Gly Asp Arg Ile Pro Ala Asp Leu
225   230   235   240

Arg Ile Ile Ser Ala Asn Gly Cys Lys Val Asp Asn Ser Ser Leu Thr
                245   250   255

Gly Glu Ser Glu Pro Gln Thr Arg Ser Pro Asp Phe Thr Asn Glu Asn
            260   265   270

Pro Leu Glu Thr Arg Asn Ile Ala Phe Phe Ser Thr Asn Cys Val Glu
        275   280   285

Gly Thr Ala Arg Gly Ile Val Val Tyr Thr Gly Asp Arg Thr Val Met
    290   295   300

Gly Arg Ile Ala Thr Leu Ala Ser Gly Leu Glu Gly Gly Gln Thr Pro
305   310   315   320

Ile Ala Ala Glu Ile Glu His Phe Ile His Ile Ile Thr Gly Val Ala
                325   330   335

Val Phe Leu Gly Val Ser Phe Phe Ile Leu Ser Leu Ile Leu Glu Tyr
            340   345   350

Thr Trp Leu Glu Ala Val Ile Phe Leu Ile Gly Ile Ile Val Ala Asn
        355   360   365

Val Pro Glu Gly Leu Leu Ala Thr Val Thr Val Cys Leu Thr Leu Thr
    370   375   380

Ala Lys Arg Met Ala Arg Lys Asn Cys Leu Val Lys Asn Leu Glu Ala
385   390   395   400

Val Glu Thr Leu Gly Ser Thr Ser Thr Ile Cys Ser Asp Lys Thr Gly
                405   410   415

Thr Leu Thr Gln Asn Arg Met Thr Val Ala His Met Trp Phe Asp Asn
            420   425   430

Gln Ile His Glu Ala Asp Thr Thr Glu Asn Gln Ser Gly Val Ser Phe
        435   440   445

Asp Lys Thr Ser Ala Thr Trp Leu Ala Leu Ser Arg Ile Ala Gly Leu
    450   455   460

Cys Asn Arg Ala Val Phe Gln Ala Asn Gln Glu Asn Leu Pro Ile Leu
465   470   475   480

Lys Arg Ala Val Ala Gly Asp Ala Ser Glu Ser Ala Leu Leu Lys Cys
                485   490   495

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Ile Glu Leu Cys Cys Gly Ser Val Lys Glu Met Arg Glu Arg Tyr Ala
                500                 505                 510

Lys Ile Val Glu Ile Pro Phe Asn Ser Thr Asn Lys Tyr Gln Leu Ser
            515                 520                 525

Ile His Lys Asn Pro Asn Thr Ser Glu Pro Gln His Leu Leu Val Met
    530                 535                 540

Lys Gly Ala Pro Glu Arg Ile Leu Asp Arg Cys Ser Ser Ile Leu Leu
545                 550                 555                 560

His Gly Lys Glu Gln Pro Leu Asp Glu Glu Leu Lys Asp Ala Phe Gln
                565                 570                 575

Asn Ala Tyr Leu Glu Leu Gly Gly Leu Gly Glu Arg Val Leu Gly Phe
            580                 585                 590

Cys His Leu Phe Leu Pro Asp Glu Gln Phe Pro Glu Gly Phe Gln Phe
        595                 600                 605

Asp Thr Asp Asp Val Asn Phe Pro Ile Asp Asn Leu Cys Phe Val Gly
    610                 615                 620

Leu Ile Ser Met Ile Asp Pro Pro Arg Ala Ala Val Pro Asp Ala Val
625                 630                 635                 640

Gly Lys Cys Arg Ser Ala Gly Ile Lys Val Ile Met Val Thr Gly Asp
                645                 650                 655

His Pro Ile Thr Ala Lys Ala Ile Ala Lys Gly Val Gly Ile Ile Ser
            660                 665                 670

Glu Gly Asn Glu Thr Val Glu Asp Ile Ala Ala Arg Leu Asn Ile Pro
        675                 680                 685

Val Ser Gln Val Asn Pro Arg Asp Ala Lys Ala Cys Val Val His Gly
    690                 695                 700

Ser Asp Leu Lys Asp Met Thr Ser Glu Gln Leu Asp Asp Ile Leu Lys
705                 710                 715                 720

Tyr His Thr Glu Ile Val Phe Ala Lys Thr Ser Pro Gln Gln Lys Leu
                725                 730                 735

Ile Ile Val Glu Arg Leu Pro Lys Thr Gly Cys Tyr Arg Gly Leu
            740                 745                 750
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<210> 746

<211> 25
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 746
Ile Pro Ala Leu Trp Xaa Ala Xaa Val Gly Arg Ser Leu Glu Pro Arg
1 5 10 15

Ser Leu Arg Ser Ala Trp Ala Thr Trp
20 25

<210> 747
<211> 37
<212> PRT
<213> Homo sapiens

<220>
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<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 747
Xaa Xaa Leu Gly Gly Arg Val Cys Ser Glu Pro Arg Trp Arg His Cys
1 5 10 15

Thr Pro Ala Trp Gly Thr Glu Arg Asp Ser Ile Ser Lys Lys Lys Lys
20 25 30

Lys Lys Ile Lys Asn
35

<210> 748

<211> 71
<212> PRT
<213> Homo sapiens

<220>
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<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (42)
<223> Xaa equals any of the naturally occurring L-amino acids

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<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 748
```
Asn Xaa Ala Leu Arg Asp Asp Val Ala Ala Gly Arg Arg Arg Leu His
  1               5                  10                  15

Ile Lys Ala Val Cys Gln Ser Val Arg Glu Ala Thr Thr Ala Ser Gly
             20                  25                  30

Gly Met Asn Ala Ala Ser Pro Arg Leu Xaa Arg His Arg Xaa Asn Gly
         35                  40                  45

Xaa Tyr Phe Thr Leu Arg Glu Arg Leu Ile Thr Met Gln Lys Gln Leu
     50                  55                  60

Gly Gly Asn Pro Glu Val Tyr
 65                  70
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<210> 749
<211> 109
<212> PRT
<213> Homo sapiens

<220>
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<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (75)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (93)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (102)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (104)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 749
Gly Ile Ser Arg Lys Met Lys Ser Ser Leu Pro Gln Gly Val Arg Asn
1 5 10 15

Val Ala Xaa Val Cys Leu Gln Ile Gly Tyr Pro Thr Val Ala Ser Val
20 25 30

Pro His Ser Ile Ile Asn Gly Tyr Xaa Arg Xaa Leu Ala Leu Ser Val
35 40 45

Glu Thr Asp Tyr Thr Phe Pro Leu Ala Glu Xaa Val Xaa Ala Ser Trp
50 55 60

Leu Ile His Leu Pro Xaa Trp Leu Leu Pro Xaa Trp Leu Leu Pro Pro
65 70 75 80

Gln Leu Leu Leu Leu Leu Leu Xaa Pro Xaa Leu Ser Xaa Asn Pro Arg
85 90 95

Lys Ser Glu Asp Pro Xaa Lys Xaa Trp Ile Gly Ser Leu
100 105

<210> 750
<211> 105
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 750
Gly Thr Xaa Gly Pro Ala Ser Gly Val Ala Gly Thr Met Gln Arg Xaa
1 5 10 15

Ser Leu Pro Phe Ala Ile Leu Thr Leu Val Asn Ala Pro Tyr Lys Arg
20 25 30

Gly Phe Tyr Cys Gly Asp Asp Ser Ile Arg Tyr Pro Tyr Arg Pro Asp
35 40 45

Thr Ile Thr His Gly Leu Met Ala Gly Val Thr Ile Thr Ala Thr Val
50 55 60

Ile Leu Val Ser Ala Gly Glu Ala Tyr Leu Val Tyr Thr Asp Arg Leu
65 70 75 80

Tyr Ser Arg Ser Asp Phe Asn Asn Tyr Val Ala Ala Val Tyr Lys Val
85 90 95

Leu Gly Thr Ser Cys Leu Gly Leu Pro
100 105

<210> 751
<211> 61
<212> PRT
<213> Homo sapiens

<220>
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<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

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<221> SITE
<222> (60)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 751
Xaa Ser Arg Lys Pro Arg Xaa Xaa Val Thr Asp Tyr Ile Lys Val Tyr
1 5 10 15

Tyr Thr Leu Arg Lys Gln Met Asn Xaa Asn Leu Phe Ser Ser Phe Ile
20 25 30

Thr Pro Thr Ile Ile Gly Leu Pro Ile Val Ile Ile Xaa Thr Met Phe
35 40 45

Pro Ser Ile Asp Xaa Pro Ile Thr Tyr Pro Xaa Xaa Gln
50 55 60

<210> 752
<211> 58
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (33)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 752
Ser Asp Pro Glu Ala Glu Val Glu Glu Ser Ser Ser Gly Leu Arg Leu
1 5 10 15

Ser Leu Ile Lys Met Thr Thr Ser Gln Lys His Arg Asp Phe Val Ala
20 25 30

Xaa Pro Met Gly Glu Asn Gln Trp Gly Thr Trp Leu Gly Leu Val Xaa
35 40 45

Ser Trp Ala Arg Asn Trp Lys Lys Gly Phe
50 55

<210> 753
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (51)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (63)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (71)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 753
Thr Leu His Ser Lys Gly Asn Lys Ser Trp Ser Ser Thr Ala Val Thr
1 5 10 15

Ala Ala Leu Glu Leu Val Gly Gly Pro Val Pro Asn Ser Pro Tyr Ser
20 25 30

Glu Ser Tyr Tyr Asn Ser Leu Ala Val Val Leu Gln Arg Arg Asp Xaa
35 40 45

Glu Asn Xaa Xaa Xaa Phe Arg Leu Val Cys Cys Val Glu Leu Xaa Ala

50 55 60

Asp Asn Asn Ser His Arg Xaa Gln Leu
65 70

<210> 754
<211> 116
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (17)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (43)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (62)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (67)
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<222> (68)
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<222> (81)
<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

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<220>
<221> SITE
<222> (91)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (92)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (101)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<220>
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<222> (112)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 754
Met Gly Ser Asp Tyr Ile Arg Glu Val Asn Val Val Lys Ser Ala Arg
1   5   10   15

Xaa Gly Tyr Ser Lys Met Leu Leu Gly Val Tyr Ala Tyr Phe Ile Glu

```
                20                  25                  30

His Lys Gln Arg Asn Thr Leu Ile Trp Leu Xaa Thr Asp Gly Asp Ala
            35                  40                  45

Arg Glu Leu Tyr Glu Lys Pro Thr Leu Ser Pro Thr Ile Xaa Asp Ile
        50                  55                  60

Pro Ser Xaa Xaa Gly Ala Gly Pro Val Val Trp Gln Lys Ser Thr Gly
 65                  70                  75                  80

Xaa Asn Lys Xaa Asn His Xaa Xaa Val Ser Xaa Xaa Trp Gly Gly Pro
                85                  90                  95

Arg Asn Pro Ile Xaa Pro Ile Ser Xaa Trp Xaa Phe Xaa Asn Ser Xaa
            100                 105                 110

Gly Pro Xaa Phe
        115
```

<210> 755
<211> 148
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (4)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (120)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (137)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (138)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (146)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 755
Ile Arg Gln Xaa Ile Asp Ile Arg Lys Asp Leu Tyr Ala Asn Asn Val
1 5 10 15

Leu Ser Gly Gly Thr Thr Met Tyr Pro Gly Ile Ala Asp Arg Met Gln
20 25 30

Lys Glu Ile Thr Ala Leu Ala Pro Ser Thr Met Lys Ile Lys Ile Ile
35 40 45

Ala Pro Pro Glu Ala Gln Ile Leu Cys Leu Asp Arg Trp Leu His Pro
50 55 60

Gly Leu Ser Val His Leu Pro Ala Asp Val Asp Gln Gln Thr Gly Asn
65 70 75 80

Thr Val Lys Pro Gly Leu Pro Leu Ser Thr Ala Asn Ala Phe Leu Lys
85 90 95

His Phe Ser Trp Phe Leu Phe Cys Leu Leu Gly Thr Gln Leu Trp Asn
100 105 110

Val Pro Val Gly Ile Tyr Gly Xaa Phe Ser Phe Phe Phe Gln Ile Ile
115 120 125

Pro Arg Ala Lys Val Leu Xaa Trp Xaa Xaa His Gly Val Phe Leu Asn
130 135 140

Lys Xaa Trp Lys
145

<210> 756
<211> 151
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (147)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 756
Ala Glu Leu Ala Thr Thr Ser Thr Met Pro Tyr Gln Tyr Pro Ala Leu

```
  1               5                  10                 15
Thr Pro Glu Gln Lys Lys Glu Leu Ser Asp Ile Ala His Arg Ile Val
            20                  25                  30
Ala Pro Gly Lys Gly Ile Leu Ala Ala Asp Glu Ser Thr Gly Ser Ile
        35                  40                  45
Ala Lys Arg Leu Gln Ser Ile Gly Thr Glu Asn Thr Glu Glu Asn Arg
    50                  55                  60
Arg Phe Tyr Arg Gln Leu Leu Leu Thr Ala Asp Asp Arg Val Asn Pro
65                  70                  75                  80
Cys Ile Gly Gly Val Ile Leu Phe His Glu Thr Leu Tyr Gln Lys Ala
                85                  90                  95
Asp Asp Gly Arg Pro Phe Pro Gln Val Ile Lys Ser Lys Gly Gly Val
            100                 105                 110
Val Gly Ile Lys Val Asp Lys Gly Val Val Pro Leu Ala Gly Thr Asn
        115                 120                 125
Gly Glu Thr Thr Thr Gln Gly Leu Asp Gly Leu Ser Glu Arg Cys Ala
    130                 135                 140
Gln Tyr Xaa Glu Gly Arg Ser
145                 150
```

<210> 757
<211> 94
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (21)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (44)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (91)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 757
Phe Val Thr Ile Leu Ser Ile Ile Ile Thr Leu Phe Phe Ile Phe Gln
1 5 10 15

Leu Lys Val Ser Xaa Tyr Ser Phe Pro Glu Asn Pro Glu Pro Lys Ser
20 25 30

Leu Thr Thr Ser Lys Ser Thr Thr Pro Trp Arg Xaa Gln Met Asn Xaa
35 40 45

Asn Leu Phe Ser Ser Phe Ile Thr Pro Thr Ile Ile Gly Leu Pro Ile
50 55 60

Val Ile Ile Ile Thr Met Phe Pro Ser Ile Ile Phe Pro Ser Pro Thr
65 70 75 80

Arg Leu Ile Asn Asn Arg Leu Ile Ser Ile Xaa Thr Met Asp
85 90

<210> 758
<211> 115
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (11)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (43)
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<220>
<221> SITE
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<220>
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<220>
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<222> (99)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 758
```
Arg Xaa Ala Leu Xaa Arg Leu Thr Ile Gly Xaa Ser Trp Tyr Ala Cys
  1               5                  10                  15

Arg Tyr Arg Ser Gly Ile Pro Gly Ser Thr His Ala Ser Xaa Arg Arg
             20                  25                  30

Gly Gln Leu Arg Ala Arg Gly Gly Gly Ala Xaa Pro Arg Gly Ala Met
         35                  40                  45

Xaa Asp Xaa Arg Ala Gly Ser Pro Arg Xaa Gly Pro Ala Ala Arg Asp
     50                  55                  60

Val Ala Ala Met Ala Ser Pro Gln Leu Cys Arg Ala Leu Val Ser Ala
 65                  70                  75                  80
```

```
Gln Trp Val Ala Glu Ala Leu Arg Ala Pro Arg Ala Gly Ala Ala Ser
                85                  90                  95

Ala Ala Xaa Arg Thr Pro Pro Gly Xaa Leu Ala Gly Ser Trp Gly Ala
            100                 105                 110

Arg Thr Xaa
        115



<210> 759
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (17)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (42)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (43)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 759
Ile Ala Xaa Gly Arg Ser Arg Gly Ser Lys Leu Thr Trp Thr Cys Met
 1               5                  10                  15

Xaa Arg His Ser Ser Ser Ile Val Ser Pro Lys Phe Asn Ser Leu Ala
            20                  25                  30

Val Val Leu Gln Arg Arg Asp Trp Glu Xaa Xaa Lys
        35                  40



<210> 760
<211> 94
<212> PRT
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<213> Homo sapiens

<220>
<221> SITE
<222> (80)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (91)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 760

```
Asn Asp Leu Val Glu Tyr Ser Pro Val Thr Glu Lys His Leu Thr Asp
  1               5                  10                  15

Gly Met Thr Val Arg Glu Leu Cys Ser Ala Ala Ile Thr Met Ser Asp
             20                  25                  30

Asn Thr Ala Ala Asn Leu Leu Leu Thr Thr Ile Gly Gly Pro Lys Glu
         35                  40                  45

Leu Thr Ala Phe Leu His Asn Met Gly Asp His Val Thr Arg Leu Asp
     50                  55                  60

Arg Trp Glu Pro Glu Leu Asn Glu Ala Ile Pro Asn Asp Glu Arg Xaa
 65                  70                  75                  80

Thr Thr Met Pro Val Ala Met Ala Thr Thr Xaa Ala Asn Tyr
                 85                  90
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<210> 761
<211> 38
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (21)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (24)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 761

```
Leu Gln Glu Ile Asn Arg Val Tyr Xaa Glu Met Tyr Lys Thr Asp Leu
 1               5                  10                  15

Glu Lys Asp Ile Xaa Ser Asp Xaa Ser Gly Asp Phe Arg Lys Leu Met
            20                  25                  30

Val Ala Leu Ala Lys Gly
        35
```

<210> 762
<211> 192
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (4)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 762

```
Cys Lys Xaa Xaa Leu Pro Ser Leu Lys Gly Thr Lys Ala Gly Ala Pro
 1               5                  10                  15

Pro Arg Cys Gly Arg Ser Arg Thr Ser Gly Ser Pro Gly Leu Gln Glu
            20                  25                  30

Phe Gly Thr Ser Cys Val Gly Leu Arg Glu Ala Val Arg Ala Gly Ala
        35                  40                  45

Val Gly Arg Gly Ala Glu Ala Leu Ala Arg Gly Met Ala His Cys Val
    50                  55                  60

Thr Leu Val Gln Leu Ser Ile Ser Cys Asp His Leu Ile Asp Lys Asp
65                  70                  75                  80

Ile Gly Ser Lys Ser Asp Pro Leu Cys Val Leu Leu Gln Asp Val Gly
                85                  90                  95

Gly Gly Ser Trp Ala Glu Leu Gly Arg Thr Glu Arg Val Arg Asn Cys
            100                 105                 110
```

Ser Ser Pro Glu Phe Ser Lys Thr Leu Gln Leu Glu Tyr Arg Phe Glu
115 120 125

Thr Val Gln Lys Leu Arg Phe Gly Ile Tyr Asp Ile Asp Asn Lys Thr
130 135 140

Pro Glu Leu Arg Asp Asp Asp Phe Leu Gly Gly Ala Glu Cys Ser Leu
145 150 155 160

Gly Gln Ile Val Ser Ser Gln Val Leu Thr Leu Pro Leu Met Leu Lys
165 170 175

Leu Glu Asn Leu Leu Gly Gly Gly Pro Ser Arg Ser Gln Leu Arg Asn
180 185 190

<210> 763
<211> 103
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (96)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 763
Ser Phe Tyr Ser Ile Pro Glu Phe Asp Glu Trp Lys Lys His Ile Glu
1 5 10 15

Asn Gln Lys Ala Trp Lys Ile Lys Tyr Tyr Lys Gly Leu Gly Thr Ser
20 25 30

Thr Ala Lys Glu Ala Lys Glu Tyr Phe Ala Asp Met Glu Arg His Arg
35 40 45

Ile Leu Phe Arg Tyr Ala Gly Pro Glu Asp Asp Ala Ala Ile Thr Leu
50 55 60

Ala Phe Ser Lys Lys Lys Ile Asp Asp Arg Lys Glu Trp Leu Thr Asn
65 70 75 80

Phe Met Glu Asp Arg Arg Gln Arg Ser Tyr Met Ala Tyr Gln Arg Xaa
85 90 95

Asp Ser Leu Ser Thr Gln Thr
100

<210> 764
<211> 105
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (101)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 764
Val Phe Ser Pro Thr Gly Ser Asp Gly Pro Leu Ala Thr Ser Lys Pro
1 5 10 15

Val Pro Ala Glu Lys Ser Gly Leu Pro Val Gly Pro Glu Asn Gly Val
20 25 30

Glu Leu Ser Lys Glu Glu Leu Ile Arg Arg Lys Arg Glu Glu Phe Ile
35 40 45

Gln Lys His Gly Arg Gly Met Glu Lys Ser Asn Lys Ser Thr Lys Ser
50 55 60

Asp Ala Pro Lys Glu Lys Gly Lys Lys Ala Pro Arg Val Trp Glu Leu
65 70 75 80

Gly Gly Cys Ala Asn Lys Glu Met Leu Asp Tyr Ser Thr Ser Thr Thr
85 90 95

Asn Gly Thr Pro Xaa Ala Cys Leu Val
100 105

<210> 765
<211> 147
<212> PRT
<213> Homo sapiens

<400> 765
Gly Arg Glu Thr Met Phe Arg Ala Ala Ala Pro Gly Gln Leu Arg Arg
1 5 10 15

Ala Ala Ser Leu Leu Arg Phe Gln Ser Thr Leu Val Ile Ala Glu His
20 25 30

Ala Asn Asp Ser Leu Ala Pro Ile Thr Leu Asn Thr Ile Thr Ala Ala
35 40 45

Thr Arg Leu Gly Gly Glu Val Ser Cys Leu Val Ala Gly Thr Lys Cys
50 55 60

Asp Lys Val Ala Gln Asp Leu Cys Lys Val Ala Gly Ile Ala Lys Val
65 70 75 80

Leu Val Ala Gln His Asp Val Tyr Lys Gly Leu Leu Pro Glu Glu Leu
85 90 95

Thr Pro Leu Ile Leu Ala Thr Gln Lys Gln Phe Asn Tyr Thr His Ile
100 105 110

Cys Ala Gly Ala Ser Ala Phe Gly Lys Asn Leu Leu Pro Arg Val Ala
115 120 125

Ala Lys Leu Glu Val Ala Pro Ile Ser Asp Ile Ile Ala Ile Lys Ser
130 135 140

Pro Asp Thr
145

<210> 766
<211> 36
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 766
Gly Arg Glu Ala Glu Ala Xaa Gln Leu Glu Ser Ser Lys Arg Phe Ala
1 5 10 15

Lys Xaa Phe Met Asp Arg His Gly Ile Pro Thr Ala Gln Trp Glu Gly
20 25 30

Phe His Gln Thr
35

<210> 767
<211> 105
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (62)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (80)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<400> 767
Arg Phe Ala Leu Ser Thr Lys Ile Pro Asp Thr Lys Gly Cys Leu Gln
1 5 10 15

Cys Arg Val Val Arg Asn Pro Tyr Thr Gly Ala Thr Phe Leu Leu Ala
20 25 30

Ala Leu Pro Thr Ser Leu Leu Leu Leu Gln Trp Tyr Glu Pro Leu Gln
35 40 45

Lys Phe Leu Leu Leu Lys Asn Phe Ser Ser Pro Leu Pro Xaa Pro Ala
50 55 60

Gly Met Leu Xaa Pro Leu Val Leu Asp Gly Lys Glu Leu Pro Gln Xaa
65 70 75 80

Phe Phe Gly Ala Glu Gly Pro Lys Gly Pro Gly Cys Arg Phe Leu Phe
85 90 95

Gln Xaa Leu Xaa Leu Gly Gly Trp Xaa
100 105

<210> 768
<211> 154
<212> PRT
<213> Homo sapiens

<400> 768
Val Thr Leu Thr Gln Cys Ser Glu Lys Leu Val Gln Leu Ile Leu His
1 5 10 15

Glu Tyr Lys Ile Phe Asn Ala Glu Val Leu Phe Arg Glu Asp Cys Ser
20 25 30

Pro Asp Glu Phe Ile Asp Val Ile Val Gly Asn Arg Val Tyr Met Pro
35 40 45

Cys Leu Tyr Val Tyr Asn Lys Ile Asp Gln Ile Ser Met Glu Glu Val
50 55 60

Asp Arg Leu Ala Arg Lys Pro Asn Ser Val Val Ile Ser Cys Gly Met
65 70 75 80

Lys Leu Asn Leu Asp Tyr Leu Leu Glu Met Leu Trp Glu Tyr Leu Ala
85 90 95

Leu Thr Cys Ile Tyr Thr Lys Lys Arg Gly Gln Arg Pro Asp Phe Thr
100 105 110

Asp Ala Ile Ile Leu Arg Lys Gly Ala Ser Val Glu His Val Gly Thr
115 120 125

Ser Thr Lys Tyr Ser Pro Gln Arg Val Gly Leu Thr His Thr Met Glu
130 135 140

His Glu Asp Val Ile Gln Ile Val Lys Lys
145 150

<210> 769
<211> 89
<212> PRT
<213> Homo sapiens

<220>
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<222> (56)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 769
Asn Gln Ala Gly Leu Thr Ala Asp Arg Met Leu Val Leu Ser Arg Ala
1 5 10 15

Gly Gln Ala Ala Gly Leu Thr Phe Asn Gln Thr Ser Glu Ser Leu Ser
20 25 30

Ala Leu Val Lys Ala Gly Val Ser Gly Glu Ala Gln Ile Ala Ser Ile
35 40 45

Ser Gln Ser Val Ala Arg Phe Xaa Ser Ala Ser Gly Val Glu Val Asp
50 55 60

Lys Val Val Glu Ala Phe Glu Gly Gly Pro Tyr Pro Phe Ala Tyr Ser
65 70 75 80

Lys Arg Ile Xaa Ile Ile Ala Val Phe
85

<210> 770
<211> 85
<212> PRT
<213> Homo sapiens

<220>
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<222> (57)
<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
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<223> Xaa equals any of the naturally occurring L-amino acids

<400> 770
Gln Thr Ser Arg Ala Glu Ser Ala Ser Met Thr Glu Arg Arg Val Pro
1 5 10 15

Phe Ser Leu Leu Arg Gly Pro Ser Trp Asp Pro Phe Arg Asp Trp Tyr
20 25 30

Pro His Ser Arg Leu Phe Asp Gln Ala Phe Gly Leu Pro Arg Leu Pro
35 40 45

Glu Glu Trp Ser Gln Trp Leu Gly Xaa Ser Ser Trp Pro Gly Tyr Val
50 55 60

Arg Pro Leu Pro Pro Ala Ala Ser Arg Ala Pro Gln Trp Pro Xaa Pro
65 70 75 80

Leu Gln Xaa Xaa Ala
85

<210> 771
<211> 76
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (50)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (70)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 771
Asp Tyr Cys Gln Val Val Arg Pro Ser Pro Ser Gly Glu Thr Ile Thr
1 5 10 15

Tyr Arg Gln Val Val Leu Ser Val Asn Val Lys Ser Pro Ala Leu Leu

20 25 30

Leu Ser Gln Leu Leu Pro Tyr Met Glu Asn Lys Lys Gly Ala Val Xaa
35 40 45

Leu Xaa Ser Ser Ile Ala Ala Tyr Asn Pro Val Val Ala Leu Gly Val
50 55 60

Tyr Asn Val Ser Lys Xaa Glu Leu Leu Gly Ser His
65 70 75

<210> 772
<211> 105
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 772
Gly Ala Glu Glu Gly Arg Gln Glu Ala Gln Gly Xaa Arg Lys Glu Ser
1 5 10 15

Tyr Ser Val Tyr Val Tyr Lys Val Leu Lys Gln Val His Pro Asp Thr
20 25 30

Gly Ile Ser Ser Lys Ala Met Gly Ile Met Asn Ser Phe Val Asn Asp
35 40 45

Ile Phe Glu Arg Ile Ala Gly Glu Ala Ser Arg Leu Ala His Tyr Asn
50 55 60

Lys Arg Ser Thr Ile Thr Ser Arg Glu Ile Gln Thr Ala Val Arg Leu
65 70 75 80

Leu Leu Pro Gly Glu Leu Ala Lys His Ala Val Ser Glu Gly Thr Lys
85 90 95

Ala Val Thr Lys Tyr Thr Ser Ala Lys
100 105

<210> 773
<211> 144
<212> PRT
<213> Homo sapiens

<220>
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<222> (98)
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<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<400> 773
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Phe Ala His Leu Pro Lys Ser Thr Phe Val Leu Asp Glu Phe Lys Arg
  1               5                  10                  15

Lys Tyr Ser Asn Glu Asp Thr Leu Ser Val Ala Leu Pro Tyr Phe Trp
             20                  25                  30

Glu His Phe Asp Lys Asp Gly Trp Ser Leu Trp Tyr Ser Glu Tyr Arg
         35                  40                  45

Phe Pro Glu Glu Leu Thr Gln Thr Phe Met Ser Cys Asn Leu Ile Thr
     50                  55                  60

Gly Met Phe Gln Arg Leu Asp Lys Leu Arg Lys Asn Ala Phe Ala Ser
 65                  70                  75                  80

Val Ile Leu Phe Gly Thr Asn Asn Ser Ser Ser Ile Ser Gly Val Trp
                 85                  90                  95

Val Xaa Pro Gly Gln Glu Leu Ala Phe Pro Leu Ser Pro Asp Trp Gln
            100                 105                 110

Val Asp Tyr Glu Val Ile His Met Ala Glu Thr Gly Ser Gly Lys Arg
        115                 120                 125
```

Gly Asp Pro Xaa Ala Gly Ser Arg Val Leu Xaa Xaa Xaa Arg Gly Pro
130 135 140

<210> 774
<211> 64
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (56)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 774
Ile Arg His Glu Arg Glu Xaa Glu Gln Gly Val Tyr Thr Cys Thr Ala
1 5 10 15

Gln Gly Ile Trp Lys Asn Glu Gln Lys Gly Glu Lys Ile Pro Arg Cys
20 25 30

Leu Pro Val Cys Gly Lys Pro Val Asn Pro Val Glu Gln Arg Gln Arg
35 40 45

Ile Ile Gly Gly Gln Lys Ala Xaa Gly Ile Val Gly Ala Phe Leu Gln
50 55 60

<210> 775
<211> 69
<212> PRT
<213> Homo sapiens

<400> 775
Asn Ile Ser Asn Ser Gln Val Asn Arg Leu Arg His Phe Val Arg Ala
1 5 10 15

Gly Leu Arg Ser Leu Phe Arg Pro Glu Pro Gln Thr Ala Val Glu Trp

```
            20                  25                  30

Ala Asp Ala Asn Tyr Tyr Leu Pro Lys Glu Ser Ala Tyr Gln Glu Gly
        35                  40                  45

Arg Trp Glu Thr Leu Pro Phe Gln Arg Ala Ile Met Asn Ala Asn Gly
    50                  55                  60

Gln Arg Leu His Pro
65



<210> 776
<211> 56
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

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<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (55)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 776
Glu Arg Val Phe Xaa Pro His Gly Leu Ile Met Asp Arg Thr Xaa Arg
 1               5                  10                  15

Phe Ala Arg Asn Val Met Lys Glu Met Gly Gly His His Ile Xaa Val
            20                  25                  30

Leu Phe Leu Leu Lys Gly Gly Tyr Lys Phe Phe Ala Asp Leu Leu Asp
```

35 40 45

Tyr Ile Lys Gly Leu Xaa Xaa Lys
50 55

<210> 777
<211> 134
<212> PRT
<213> Homo sapiens

<220>
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<222> (4)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 777
Leu Gln Phe Xaa Xaa Xaa Met Ile Thr Pro Ser Ser Asn Thr Thr His
1 5 10 15

Tyr Arg Glu Ser Trp Tyr Ala Cys Arg Tyr Arg Ser Gly Ile Pro Gly
20 25 30

Ser Thr His Ala Ser Gly Val Phe Glu Val His Lys Lys Asn Val Arg
35 40 45

Gly Glu Phe Thr Tyr Tyr Glu Ile Gln Asp Asn Thr Gly Lys Met Glu
50 55 60

Val Val Val His Gly Arg Leu Thr Thr Ile Asn Cys Glu Glu Gly Asp
65 70 75 80

Lys Leu Lys Leu Thr Cys Phe Glu Leu Ala Pro Lys Ser Gly Asn Thr
85 90 95

Gly Glu Leu Arg Ser Val Ile His Ser His Ile Lys Val Ile Lys Thr
100 105 110

Arg Lys Asn Lys Lys Asp Ile Leu Asn Pro Asp Ser Ser Met Glu Thr
115 120 125

Ser Pro Asp Phe Phe Phe
130

<210> 778
<211> 133
<212> PRT
<213> Homo sapiens

<400> 778
Thr Ile Thr Ser Gly Gly Asn Pro Pro Ala Phe Ser Leu Thr Pro Asp
1 5 10 15

Gly Lys Leu Thr Ala Lys Asn Ala Asp Ile Ser Gly Ser Val Asn Ala
20 25 30

Asn Ser Gly Thr Leu Ser Asn Val Thr Ile Ala Glu Asn Cys Thr Ile
35 40 45

Asn Gly Thr Leu Arg Ala Glu Lys Ile Val Gly Asp Ile Val Lys Ala
50 55 60

Ala Ser Ala Ala Phe Pro Arg Gln Val Glu Ser Ser Val Asp Trp Pro
65 70 75 80

Ser Gly Thr Arg Thr Val Thr Val Thr Asp Asp His Pro Phe Asp Arg
85 90 95

Gln Ile Val Val Leu Pro Leu Thr Phe Arg Gly Ser Lys Arg Thr Val
100 105 110

Ser Gly Arg Thr Thr Tyr Ser Met Cys Tyr Leu Lys Val Leu Met Asn
115 120 125

Gly Ala Val Ile Tyr
130

<210> 779
<211> 90
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (52)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (63)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 779
Pro Asn Thr Ala Leu Val Gly Val Gln Val Asp Ser Glu Gln Phe Gly
1 5 10 15

Ser Gln Gln Val Ser Arg Asn Tyr His Leu Arg Gly Arg Ile Leu Gln
20 25 30

Val Pro Ser Asn Tyr Asn Pro Gln Thr Arg Gln Tyr Ser Gly Ile Trp
35 40 45

Asp Gly Thr Xaa Lys Pro Ala Tyr Ser Asn Asn Met Ala Trp Xaa Leu
50 55 60

Trp Asp Met Leu Thr His Pro Arg Tyr Gly Met Gly Lys Arg Leu Gly
65 70 75 80

Ala Ala Asp Val Asp Lys Trp Ala Leu Tyr
85 90

<210> 780
<211> 82
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (14)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

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<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (73)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 780
Val Xaa Arg Ala Ser Asp Asp Ala Glu Gly Tyr Leu Asp Xaa Phe Lys
1 5 10 15

Gly Lys Ile Thr Glu Ser His Leu Xaa Lys Glu Leu Leu Glu Lys Val
20 25 30

Glu Leu Thr Glu Asp Asn Ala Ser Arg Leu Glu Glu Phe Ser Lys Xaa
35 40 45

Trp Lys Asp Ala Ser Xaa Lys Trp Asn Ala Met Trp Ala Xaa Lys Ile
50 55 60

Xaa Gln Thr Lys Asp Xaa Lys Arg Xaa Leu Phe Cys Tyr Leu Val Val
65 70 75 80

Arg Ser

<210> 781
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (43)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 781
Pro Asp Phe His Arg Glu Asp Asp Trp Trp Arg Asn Gly Gln Asn Leu
1 5 10 15

Tyr Leu Asp Asn Leu Glu Ala Thr Gly Leu Tyr Gln Val Pro Leu Ser
20 25 30

Ala Ala Gln Pro Gly Asp Val Leu Leu Cys Xaa Phe Gly Ser Ser Xaa
35 40 45

Xaa

<210> 782
<211> 85
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 782
Xaa Lys Glu Asn Gly Thr Val Thr Ala Ala Asn Ala Ser Thr Leu Asn
1 5 10 15

Asp Gly Ala Ala Ala Leu Val Leu Met Thr Ala Asp Ala Ala Xaa Arg
20 25 30

```
Leu Asn Val Thr Pro Leu Ala Arg Ile Val Ala Phe Ala Asp Ala Ala
        35                  40                  45

Val Glu Pro Ile Asp Phe Pro Ile Ala Pro Val Tyr Ala Ala Ser Met
    50                  55                  60

Val Leu Lys Asp Val Gly Leu Lys Lys Glu Asp Ile Ala Met Trp Glu
65                  70                  75                  80

Val Asn Gly Ser Leu
                85
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<210> 783
<211> 90
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (14)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (27)
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (44)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (63)
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<220>
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<222> (81)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (87)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 783
Gly Lys Ser Pro Ala Ser Trp Trp Gly Ser Ala Gly His Xaa Xaa Xaa
1 5 10 15

Pro Cys Arg Gly Ala Cys Ala Ala Ala Gly Xaa Thr Ala Xaa Arg Gly
20 25 30

Phe Ala Val Ser Ala Arg Xaa Val Trp Gln Thr Xaa Asp Arg Pro Gly
35 40 45

Thr Trp Asp Gln Ser Arg Asn Leu Leu Leu Asn Gly Lys Ser Xaa Pro
50 55 60

Thr Lys Val Arg Leu Ile Trp Gly Gly Ser Leu Pro Pro Val Lys Arg
65 70 75 80

Xaa Ala Asp Glu Leu Asp Xaa Arg Pro Gly
85 90

<210> 784
<211> 84
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (64)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (70)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (79)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (81)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 784
Ala Leu Leu Gly Leu Thr Ile Xaa Lys Ala Gly Thr Pro Ala Gly Thr
1   5   10   15

Gly Pro Glu Phe Pro Gly Arg Pro Thr Arg Pro Leu Leu Cys Leu Glu
            20   25   30

Gly Ile Ile Leu Ser Leu Phe Val Ile Ile Thr Ile Thr Ile Leu Ile
        35   40   45

Asn His Leu Thr Leu Ala Ser Ile Thr Pro Ile Ile Leu Leu Val Xaa
    50   55   60

Ala Ala Cys Glu Ala Xaa Leu Gly Leu Ile Pro Phe Ser Tyr Xaa Leu
65   70   75   80

Xaa Tyr Ile Arg

<210> 785
<211> 61
<212> PRT
<213> Homo sapiens

<400> 785
Ile Gly Phe Asp Asn Lys Lys Asp Leu Leu Ile Ser Val Gly Asp Leu
1   5   10   15

Val Asp Arg Gly Ala Glu Asn Val Glu Cys Leu Glu Leu Ile Thr Phe
            20   25   30

Pro Trp Phe Arg Ala Val Arg Gly Asn His Glu Gln Met Met Ile Asp
35 40 45

Gly Leu Ser Glu Arg Gly Asn Val Asn His Trp Leu Leu
50 55 60

<210> 786
<211> 102
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (33)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (64)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (83)
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<220>
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<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (86)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 786
Gly Leu Gln Pro Tyr Cys Tyr Xaa Thr Trp Arg Cys Arg Cys Thr Thr
1 5 10 15

Gly Gln Pro Gly Thr Ala Pro Ala Gly Thr Pro Gly Ala Pro Pro Leu
20 25 30

```
Xaa Gly Met Ala Ile Val Lys Glu Glu Glu Thr Glu Ala Ala Ile Gly
        35                  40                  45

Ala Pro Pro Thr Ala Thr Glu Gly Pro Glu Thr Lys Pro Val Leu Xaa
    50                  55                  60

Ala Leu Glu Glu Gly Pro Gly Ala Glu Gly Ser Arg Leu Asp Ser Leu
65                  70                  75                  80

Val Ala Xaa Xaa Leu Xaa Leu Glu Val Val Ala Leu Arg Asp Ser Ala
                85                  90                  95

Pro Val Leu Ala Gly Thr
            100



<210> 787
<211> 64
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (44)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 787
Cys Leu Xaa Arg Ala Arg Xaa Pro Ala Ala Ala Asn Ser Ser Gly Asp
 1               5                  10                  15

Gly Gly Ala Ala Gly Asp Gly Thr Val Val Asp Cys Pro Val Cys Lys
            20                  25                  30

Gln Gln Cys Phe Ser Lys Asp Ile Val Glu Asn Xaa Phe Met Arg Xaa
        35                  40                  45
```

Ser Gly Ser Lys Ala Ala Thr Asp Ala Gln Asp Ala Asn Gln Cys Cys
50 55 60

<210> 788
<211> 61
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (52)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 788
Thr Leu Ala Phe Phe Leu Ile Pro Cys Ile Gly Ser Pro Ala Cys Pro
1 5 10 15

Thr Met Ser Asp Ala Ala Val Asp Thr Ser Ser Glu Ile Thr Thr Lys
20 25 30

Asp Leu Lys Glu Lys Lys Glu Val Leu Glu Arg Gly Arg Lys Trp Lys
35 40 45

Arg Arg Pro Xaa Leu Thr Gly Asn Ala Asn Leu Gly Lys
50 55 60

<210> 789
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 789
Ala Gln Asp Asn Phe Lys His Leu Asn Gly Ile Xaa Leu Phe His Cys
1 5 10 15

Ile Asp Pro Asn Gly Ser Lys His Lys Arg Thr Asp Arg Ser Ile Leu
20 25 30

```
Cys Cys Leu Arg Lys Gly Glu Ser Gly Gln Ser Trp Gln Gly Leu Thr
        35                  40                  45

Lys Glu Arg Ala Lys Leu Asn Trp Leu Ser Val Asp Phe Asn Asn Trp
    50                  55                  60

Glu Arg Leu Gly Arg
65
```

<210> 790
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (22)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (24)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 790

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Gln Ser Thr Val Lys Leu Glu His Ala Lys Ser Val Ala Ser Arg Ala
  1               5                  10                  15

Thr Val Leu Gln Lys Xaa Ser Xaa Thr Pro Val Gly Met Phe Leu Lys
             20                  25                  30

Leu Asn Xaa Met Asn Val Lys Phe Xaa Ser Gly Tyr Tyr Glu Leu Pro
        35                  40                  45

Cys Arg Ser
    50
```

<210> 791
<211> 154
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 791
Asp Pro Gln Ala His Val Ala Met Leu Ser Ser Thr Ala Met Tyr Ser
1 5 10 15

Ala Pro Gly Arg Asp Leu Gly Met Glu Pro His Arg Ala Ala Gly Pro
20 25 30

Leu Gln Leu Arg Phe Ser Pro Tyr Val Phe Asn Gly Gly Thr Ile Leu
35 40 45

Ala Ile Ala Gly Glu Asp Phe Ala Ile Val Ala Ser Asp Thr Arg Leu
50 55 60

Ser Glu Gly Phe Ser Ile His Thr Arg Asp Ser Pro Lys Xaa Tyr Lys
65 70 75 80

Leu Thr Asp Lys Thr Val Ile Gly Cys Ser Gly Phe His Gly Asp Cys
85 90 95

Leu Thr Leu Thr Lys Ile Ile Glu Ala Arg Leu Lys Met Tyr Lys His
100 105 110

Ser Asn Asn Lys Ala Met Thr Thr Gly Ala Ile Ala Ala Met Leu Ser
115 120 125

Thr Ile Leu Tyr Ser Arg Arg Phe Phe Pro Tyr Tyr Val Tyr Asn Ile
130 135 140

Ile Gly Gly Leu Asp Glu Glu Gly Lys Gly
145 150

<210> 792
<211> 96
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (73)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (74)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 792
Gly Thr Ala Ser Thr Ala Met Tyr Ser Ala Pro Gly Arg Asp Leu Gly
1 5 10 15

Met Glu Pro His Arg Ala Ala Gly Pro Leu Gln Leu Arg Phe Ser Pro
20 25 30

Tyr Val Phe Asn Gly Gly Thr Ile Leu Ala Ile Ala Gly Glu Asp Phe
35 40 45

Ala Ile Val Ala Ser Asp Thr Arg Leu Ser Glu Gly Phe Ser Ile His
50 55 60

Thr Arg Asp Ser Pro Lys Cys Xaa Xaa Xaa Asn Arg Gln Asn Ser His
65 70 75 80

Trp Met Gln Arg Phe Ser Trp Arg Leu Ser Tyr Ala Asp Lys Asp Tyr
85 90 95

<210> 793
<211> 72
<212> PRT
<213> Homo sapiens

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<400> 793
Arg Pro Pro Val Arg Xaa Phe Leu Arg Asp Phe Phe Met Ser Met Tyr
1 5 10 15

Thr Thr Ala Gln Leu Leu Ala Ala Asn Glu Gln Lys Phe Lys Phe Asp

20 25 30

Pro Leu Phe Leu Arg Leu Phe Phe Arg Glu Ser Tyr Pro Phe Thr Thr
35 40 45

Glu Glu Ser Leu Ser Leu Thr Asn Ser Gly Thr Gly Lys His Gly Ala
50 55 60

Val Arg Phe Ala Asp Cys Phe Arg
65 70

<210> 794
<211> 124
<212> PRT
<213> Homo sapiens

<400> 794
Gly Ser Gly Asp His Glu Gly Gly Lys Gly Asp Gly Met Glu Glu Val
1 5 10 15

Pro His Asp Cys Pro Gly Ala Asp Ser Ala Gln Ala Gly Arg Gly Ala
20 25 30

Ser Cys Gln Gly Cys Pro Asn Gln Arg Leu Cys Ala Ser Gly Ala Gly
35 40 45

Ala Thr Pro Asp Thr Ala Ile Glu Glu Ile Lys Glu Lys Met Lys Thr
50 55 60

Val Lys His Lys Ile Leu Val Leu Ser Gly Lys Gly Gly Val Gly Lys
65 70 75 80

Ser Thr Phe Ser Ala His Leu Ala His Gly Leu Ala Glu Asp Glu Asn
85 90 95

Thr Gln Ile Ala Leu Leu Asp Ile Asp Ile Cys Gly Pro Ser Ile Pro
100 105 110

Lys Ile Met Gly Leu Glu Gly Glu Gln Val His Gln
115 120

<210> 795
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<212> PRT
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<400> 795
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Ala Arg Xaa Trp Leu Xaa Gly Val Thr Phe Xaa Val Thr Thr Val Xaa
  1               5                  10                  15

Thr Lys Xaa Arg Thr Glu Xaa Val Gln Lys Leu Cys Pro Gly Gly Gln
             20                  25                  30

Xaa Pro Phe Leu Leu Tyr Xaa Thr Glu Val His Thr Asp Thr Asn Lys
         35                  40                  45

Xaa Ala Glu Phe Leu Xaa Ala Val Leu Cys Pro Pro Arg Tyr Pro Xaa
     50                  55                  60

Leu Ala Ala Leu Asn Pro Xaa Ser Asn Thr Ala Xaa Leu Xaa Ile Phe
```

65 70 75 80

Xaa Lys Xaa Ser Ala Tyr Xaa Xaa Xaa Ser Asn Pro Xaa Leu Asn Asp
85 90 95

Asn Leu Glu Xaa Gly Leu Leu Lys Ala Leu Xaa Val Leu Xaa Asn Xaa
100 105 110

Leu Thr Ser Pro Xaa Ser Glu Glu Val Asp Xaa Thr Ser Ala Xaa Val
115 120 125

Lys Val Ser Leu Arg Arg Ser Xaa Trp Ile Ala Arg Ala His Pro Gly
130 135 140

<210> 796
<211> 97
<212> PRT
<213> Homo sapiens

<220>
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<222> (31)
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<400> 796
Ile Met Lys Asn Gly Phe Tyr Ala Thr Tyr Arg Ser Lys Asn Lys Gly
1 5 10 15

Lys Asp Lys Arg Ser Ile Asn Leu Ser Val Phe Leu Asn Ser Xaa Leu
20 25 30

Ala Asp Asn His His Leu Gln Val Gly Ser Asn Tyr Leu Tyr Ile His
35 40 45

Lys Ile Asp Gly Lys Thr Phe Leu Phe Thr Lys Thr Asn Asp Lys Ser
50 55 60

Leu Val Gln Lys Ile Asn Arg Ser Lys Ala Ser Val Glu Asp Ile Lys
65 70 75 80

Asn Ser Leu Val Asp Asp Gly Ile Ile Gly Ile Pro Ile Phe Phe Val
85 90 95

Cys

<210> 797
<211> 181
<212> PRT
<213> Homo sapiens

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<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<400> 797

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Arg Xaa Xaa Pro Ser Leu Lys Gly Thr Lys Ala Gly Ala Pro Pro Arg
 1               5                  10                  15

Cys Gly Arg Ser Arg Thr Ser Gly Ser Pro Gly Leu Gln Glu Phe Gly
            20                  25                  30

Thr Arg Pro Ser Arg Leu Arg Lys Thr Arg Lys Leu Arg Gly His Val
        35                  40                  45

Ser His Gly His Gly Arg Ile Gly Lys His Arg Lys His Pro Gly Gly
    50                  55                  60

Arg Gly Asn Ala Gly Gly Leu His His His Arg Ile Asn Phe Asp Lys
65                  70                  75                  80

Tyr His Pro Gly Tyr Phe Gly Lys Val Gly Met Lys His Tyr His Leu
                85                  90                  95

Lys Arg Asn Gln Ser Phe Cys Pro Thr Val Asn Leu Asp Lys Leu Trp
            100                 105                 110

Thr Leu Val Ser Glu Gln Thr Arg Val Asn Ala Ala Lys Asn Lys Thr
        115                 120                 125

Gly Ala Ala Pro Ile Ile Asp Val Val Arg Ser Gly Tyr Tyr Lys Val
    130                 135                 140

Leu Gly Lys Gly Lys Leu Pro Lys Gln Pro Val Ile Val Lys Ala Lys
145                 150                 155                 160

Phe Phe Ser Arg Arg Ala Glu Glu Lys Ile Lys Ser Val Gly Gly Ala
                165                 170                 175
```

Cys Val Leu Val Ala
180

<210> 798
<211> 136
<212> PRT
<213> Homo sapiens

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<222> (29)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 798
Trp Ile Pro Arg Ala Ala Gly Ile Arg His Glu Arg Lys Glu Gly Trp
1 5 10 15

Arg Glu Glu Lys Gly Pro Phe Cys His Gln Arg Arg Xaa Thr Arg Glu
20 25 30

Tyr Thr Ile Asn Ile His Lys Arg Ile His Gly Val Gly Phe Lys Lys
35 40 45

Arg Ala Pro Arg Ala Leu Lys Glu Ile Arg Lys Phe Ala Met Lys Glu
50 55 60

Met Gly Thr Pro Asp Val Arg Ile Asp Thr Arg Leu Asn Lys Ala Val
65 70 75 80

Trp Ala Lys Gly Ile Arg Asn Val Pro Tyr Arg Ile Arg Val Arg Leu
85 90 95

Ser Arg Lys Arg Asn Glu Asp Glu Asp Ser Pro Asn Lys Leu Tyr Thr
100 105 110

Leu Val Thr Tyr Val Pro Val Thr Thr Phe Lys Ile Ser Val Leu Asn
115 120 125

Ser Val Thr Val Ala Lys Ser Pro
130 135

<210> 799
<211> 142
<212> PRT
<213> Homo sapiens

<400> 799

Trp Ile Pro Arg Ala Ala Gly Ile Arg His Glu Ala Ala Leu Ala Ala
1 5 10 15

Cys Ala Ala Met Ala Lys Ile Lys Ala Arg Asp Leu Arg Gly Lys Lys
20 25 30

Lys Glu Glu Leu Leu Lys Gln Leu Asp Asp Leu Lys Val Glu Leu Ser
35 40 45

Gln Leu Arg Val Ala Lys Val Thr Gly Gly Ala Ala Ser Lys Leu Ser
50 55 60

Lys Ile Arg Val Val Arg Lys Ser Ile Ala Arg Val Leu Thr Val Ile
65 70 75 80

Asn Gln Thr Gln Lys Glu Asn Leu Arg Lys Phe Tyr Lys Gly Lys Lys
85 90 95

Tyr Lys Pro Leu Asp Leu Arg Pro Lys Lys Thr Arg Ala Met Arg Arg
100 105 110

Arg Leu Asn Lys His Glu Glu Asn Leu Lys Thr Lys Lys Gln Gln Arg
115 120 125

Lys Glu Arg Leu Tyr Pro Leu Arg Lys Tyr Ala Val Lys Ala
130 135 140

<210> 800
<211> 74
<212> PRT
<213> Homo sapiens

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<400> 800
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Xaa Xaa Tyr His Lys Tyr Lys Ala Lys Arg Asn Cys Trp Xaa Xaa Val
  1               5                  10                  15

Arg Gly Val Xaa Met Asn Pro Val Glu His Pro Phe Gly Gly Gly Asn
             20                  25                  30

His Gln His Ile Gly Lys Pro Ser Thr Ile Arg Arg Asp Ala Pro Ala
         35                  40                  45

Gly Arg Lys Val Gly Leu Ile Ala Ala Xaa Xaa Xaa Gly Xaa Leu Xaa
     50                  55                  60
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Gly Thr Lys Xaa Val Gln Glu Lys Glu Asn
 65                 70


<210> 801
<211> 100
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 801
Met Thr Pro Val Gln Arg Gly Gly Pro Gly Ala Xaa Val Ala Leu Gly
  1               5                  10                  15

Trp Gly Thr Ala Val Ala Ser Ala Arg Phe Arg Gln Trp His Pro Gly
             20                  25                  30

Pro Gly Ser Arg Pro Trp Thr Gly Pro Gly Pro Arg Pro Arg Thr Arg
         35                  40                  45

Xaa Gly Lys Ala Glu Asp Lys Glu Trp Met Pro Val Thr Lys Leu Gly
     50                  55                  60

Arg Leu Val Lys Asp Met Lys Ile Lys Ser Leu Glu Glu Ile Tyr Leu
 65                  70                  75                  80

Phe Ser Leu Pro Ile Lys Glu Ser Glu Ile Ile Asp Ser Ser Trp Gly
                 85                  90                  95

Leu Ser Gln Gly
            100


<210> 802
<211> 19
<212> PRT
<213> Homo sapiens

<220>
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<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 802
Xaa Glu Thr Gln Ala Ile Val Cys Gln Gln Leu Asp Leu Thr His Leu
1 5 10 15

Lys Gly Ala

<210> 803
<211> 54
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 803
Gly Thr Arg Asp Val Arg Arg Val Pro Gly Val Ala Pro Thr Leu Val
1 5 10 15

Arg Ser Ala Ser Glu Thr Ser Glu Lys Arg Pro Phe Met Cys Ala Tyr
20 25 30

Pro Gly Cys Asn Lys Arg Tyr Phe Lys Leu Ser His Leu Gln Met His
35 40 45

Ser Arg Xaa Ala His Trp
50

<210> 804
<211> 140
<212> PRT
<213> Homo sapiens

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<220>
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<222> (136)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 804
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Phe Lys Ser Tyr Leu Gly Asp Thr Ile Glu Gly Ser Leu Gln Val Thr
  1               5                  10                  15

Gly Pro Glu Ile Pro Gly Ser Thr His Ala Ser Ala Glu Ser Leu Ser
             20                  25                  30

Arg Arg Lys Leu Asp Thr Gly Thr Gly Ser Ala Met Arg Leu Leu Pro
         35                  40                  45

Arg Leu Leu Leu Leu Leu Leu Leu Val Phe Pro Ala Thr Val Leu Phe
     50                  55                  60

Arg Gly Gly Pro Arg Gly Leu Leu Ala Val Ala Gln Asp Leu Thr Glu
 65                  70                  75                  80

Asp Glu Glu Thr Val Glu Asp Ser Ile Ile Glu Asp Glu Asp Asp Glu
                 85                  90                  95

Ala Xaa Val Glu Glu Asp Glu Xaa Thr Asp Phe Val Glu Asp Lys Glu
            100                 105                 110

Glu Glu Asp Val Ser Gly Glu Xaa Glu Thr Leu Pro Ser Ala Asp Thr
        115                 120                 125

Thr Ile Leu Phe Leu Lys Xaa Xaa Ile Phe Arg Gln
    130                 135                 140
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<210> 805
<211> 130
<212> PRT
<213> Homo sapiens

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<400> 805
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Phe Glu Ala Asn Arg Gln Arg Ala Thr Met Ala Val Ala Arg Ala Ala
  1               5                  10                  15

Leu Gly Pro Leu Val Thr Gly Leu Tyr Asp Val Gln Ala Phe Lys Phe
             20                  25                  30

Gly Asp Phe Val Leu Lys Ser Gly Leu Ser Ser Pro Ile Tyr Ile Asp
         35                  40                  45

Leu Arg Gly Ile Val Ser Arg Pro Arg Leu Leu Ser Gln Val Ala Asp
     50                  55                  60

Ile Leu Phe Gln Thr Ala Gln Asn Ala Gly Ile Ser Phe Asp Thr Val
 65                  70                  75                  80

Cys Gly Val Pro Tyr Thr Ala Leu Pro Leu Ala Thr Val Ile Cys Ser
                 85                  90                  95

Thr Asn Gln Ile Pro Met Leu Ile Xaa Arg Lys Glu Thr Lys Asp Tyr
            100                 105                 110

Gly Thr Lys Arg Leu Val Xaa Xaa Ile Leu Ile Xaa Xaa Lys Leu Phe
        115                 120                 125

Asn His
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130

<210> 806
<211> 35
<212> PRT
<213> Homo sapiens

<400> 806
Val Ala Asp Ile Ala Trp Trp Phe Arg Arg Arg Ile Phe Ile Ala Val
1 5 10 15

Leu Arg Cys Asn Ser Ser Ile Ser Asp Ala Glu Ser Met Met Ser Ala
20 25 30

Ile Phe His
35

<210> 807
<211> 72
<212> PRT
<213> Homo sapiens

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<400> 807
Asp Trp Arg Gln Thr Ser Xaa Ser Gly Ala His Gly Arg Leu Lys Pro
1 5 10 15

Trp Xaa Asn Pro Xaa Ala Arg Arg Asp Ala Arg Glu Asp Arg Ala Thr
20 25 30

Trp Lys Ser Asn Tyr Xaa Leu Lys Ile Xaa Gln Arg Ile Gly Met Ile
35 40 45

Ile Leu Lys Trp Val Xaa Leu Val Gly Ser Glu Tyr Xaa Met Val Gly
50 55 60

Xaa Pro Xaa Xaa Ser Met Ala Ser
65 70

<210> 808
<211> 53
<212> PRT
<213> Homo sapiens

<220>
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<222> (30)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (52)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 808
Pro Ser Leu Lys Gly Thr Lys Ala Gly Asn Asp Leu Val Ser Leu Arg
1 5 10 15

Ala Ala Arg Thr Leu Arg Pro Pro Gly Thr Lys Pro Gly Xaa Gly Ala
20 25 30

Thr Phe Gly Pro Gly Leu Ser Glu Arg Ala Ser Ala Gln Arg Gly Ser
35 40 45

Gly Gln Leu Xaa His
50

<210> 809
<211> 70
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<220>
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<220>
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<220>
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<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (53)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 809
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Ala Xaa Glu Tyr Thr Leu Arg Thr Ser Gly Leu Thr Val Arg Pro Xaa
  1               5                  10                  15

Thr Ser Gly Pro Gly Cys Xaa Cys Gln Gly Gly Leu Ser Asp Leu Arg
             20                  25                  30

Met Gly Xaa Met Glu Trp Xaa Arg Arg Asp Ala Gly Val Xaa Ala Gly
         35                  40                  45

Xaa Asp Arg Ser Xaa Thr His Glu Cys Gln Val Gln Val Val Arg Val
     50                  55                  60

Gly Asp Met Ser Leu Glu
 65                  70
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<210> 810
<211> 39
<212> PRT
<213> Homo sapiens

<220>
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<222> (1)
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<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (4)
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<220>
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<220>
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<222> (22)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (39)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 810
Xaa Ile Xaa Xaa Cys Gly Phe Glu Pro Pro His Phe Leu Thr Leu Asn
1 5 10 15

Leu Xaa Met His Arg Xaa Ser Cys Pro Leu Asp Cys Lys Val Tyr Val
20 25 30

Gly Ile Leu Gly Thr Met Xaa
35

<210> 811
<211> 27
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (22)
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<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 811

Gly Arg Glu Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
1 5 10 15

Lys Lys Lys Lys Lys Xaa Pro Xaa Xaa Gly Pro
20 25

<210> 812
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (4)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (21)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 812
Arg Arg Arg Xaa Arg Pro Ala Pro Pro Pro Gly Ala Cys Leu His Leu
1 5 10 15

Arg Leu Pro Lys Xaa Leu Gly Gln Arg Leu Asp Ala Arg His Gln Gly
20 25 30

Pro Val Glu Val Leu Gln Glu Glu Arg Arg Pro Arg Pro Arg Leu Pro
35 40 45

Arg Pro Ala Leu Ala Thr Leu Ser Ala Arg Phe Thr Asn Lys Leu Ser
50 55 60

Asp Pro Lys Lys Lys Lys Lys Lys
65 70

<210> 813
<211> 27
<212> PRT
<213> Homo sapiens

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 813
Asn Ser Ala Xaa Xaa Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
1 5 10 15

Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
20 25

<210> 814
<211> 23
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (23)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 814
Asn Ser Ala Gln Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
1 5 10 15

Lys Lys Lys Lys Lys Lys Xaa
20

<210> 815
<211> 46
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (16)
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<220>
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<222> (46)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 815
Phe Asp Gln Arg Thr Arg Ile Thr Arg Pro Gln Arg Arg Val Phe Xaa
1   5   10   15

Ala Ser Xaa Ser Pro Pro Lys Xaa Ile Thr Asn Cys Ile Tyr Xaa Lys
            20   25   30

Ile Asn Arg Tyr Xaa Xaa Leu Asn Ile Ala Ile Gln Ile Xaa
        35   40   45

<210> 816
<211> 52
<212> PRT
<213> Homo sapiens

<220>
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<222> (4)
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Lys Arg Met Lys Met Xaa Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
20 25 30

Lys Lys Lys Lys Lys Lys Lys Lys Xaa Pro Gly Gly Xaa Pro Pro Pro
35 40 45

Pro Xaa Pro Pro
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<210> 817
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Pro Gln Leu Gly Lys Arg His Met Ser Leu Ala Xaa Pro Ile Ala Asn
20 25 30

Pro Val Val Gly Phe Leu Ala Tyr Ser Arg Pro Ser Val Leu Pro Gly
35 40 45

Trp His Arg Pro His Arg Thr Ser Arg Val Gly Leu Ser Gly Ser Ser
50 55 60

Thr Ala Gly Xaa Xaa Asn Ser Arg Phe Gly Gly Cys Ser Phe Gln Ala
65 70 75 80

Gly Asp Thr Leu Gly Pro Val Val Arg Ser Pro Val Leu Arg His Leu
85 90 95

Val Trp Asn Xaa Arg Leu Ala Val Ser Ile Gly Val Gly Xaa Cys Ala
100 105 110

Ala

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<400> 818

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Asn Gln Asn Gln Asn Pro Xaa Gln Ser Ile Xaa Lys Ser Lys Pro Gly
             20                  25                  30

Gln Asn Gln Asn Glu Xaa Xaa Lys Gln Ser Lys Ser Ser Gln Lys Gln
         35                  40                  45

Lys Pro Lys Cys Arg Tyr Arg Xaa Xaa Val Gly Asp Gln Ala Thr Leu
     50                  55                  60

Pro Leu Lys Trp Ser Gly Xaa Xaa Pro Lys Thr Ser Xaa Thr Xaa Phe
 65                  70                  75                  80

Xaa Xaa Ser Gly Xaa Gln Xaa Pro Val Pro Ser Gln Xaa Xaa Ala Ala
                 85                  90                  95

Xaa Leu Ile Leu Cys Gly Gly Leu Xaa Asn Ala Xaa Leu Ala Arg Cys
            100                 105                 110

Ser Thr Gly Xaa Ile Ala Tyr Pro Xaa Val Leu Ser Gly Ser Xaa Ser
        115                 120                 125

Leu Lys Leu Ala
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<210> 819
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<400> 819
Asn Ser Ala Xaa Gln Thr Thr Pro Ser Leu Ser Tyr Val Phe Leu Leu
1 5 10 15

Gln Thr Thr Arg Gln Leu Leu Lys Pro Ala Ile His Val Tyr Phe Asn
20 25 30

Lys Leu Met Ala Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
35 40 45

Lys Lys Lys Lys Lys Xaa Xaa Gly Gly Gly Pro Pro Pro Pro
50 55 60

<210> 820
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Asp His Thr Ser Asp Thr Xaa Ala Trp Val Thr Glu Arg Asp Ser Val
1 5 10 15

Xaa Gly Lys Glu Lys Lys Lys Lys Lys Xaa Xaa Gly Gly Ala Pro Val
20 25 30

Pro Asn Trp Pro Tyr Xaa Gly Ser
35 40

<210> 821
<211> 64
<212> PRT
<213> Homo sapiens

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<400> 821
Ala Xaa Pro Thr Gln Gln Ser Phe Pro Gln Leu Pro Arg Arg Lys Gly
1 5 10 15

Pro Ser Trp Val Trp Asp His Lys Gly Gly Asp Cys Thr Pro Leu Pro
20 25 30

Leu Gly Pro Gly Cys Gly Gln Arg Pro Pro Cys Val Ser Arg Val Thr
35 40 45

Val Pro Leu Ser Cys Asp Ala Ile Ser Val Cys Ala Trp Ser Pro Gln
50 55 60

<210> 822
<211> 61
<212> PRT
<213> Homo sapiens

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<400> 822
His Leu Cys Phe Lys Trp Gly Ser Pro Cys Arg Gly Phe Ile Gly His
1 5 10 15

Trp Leu Ser Lys Cys Gln Xaa Trp Ala Gly Gly Gly Thr Glu Pro Pro
20 25 30

Gln His Cys Ala Leu Val Glu Lys Ala Leu Thr Cys His Ala Pro Leu
35 40 45

Lys Pro Pro Leu Leu Thr Cys Leu Leu His Pro Ser His
50 55 60

<210> 823
<211> 73
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<400> 823
Thr Ala Gly Arg Trp Pro Trp Lys Ser Glu Ser Ala Lys Glu Cys Val
1 5 10 15

Thr Thr His Leu Pro Asn Gln Leu Ala Leu Lys Met Asp Gly Ala Gly
20 25 30

Ala Ser Gly Pro Tyr Pro Ser Val Ala Gly Ser Arg Glu Trp Thr Gly
35 40 45

Xaa Ala Gly Ala Ala Arg Ala Arg Xaa Val Met Val Cys Val Gly Gly
50 55 60

Arg Arg Arg Arg Arg Gly Cys Xaa Val
65 70

<210> 824
<211> 34
<212> PRT
<213> Homo sapiens

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<400> 824
Pro Arg Xaa Arg Arg Gln Gln Gln Pro His His Xaa Val Ala Asp Gly
1 5 10 15

Pro His Ala Gly Gly Pro Leu Pro Ala Leu Xaa Arg Arg Leu Xaa Leu
20 25 30

Pro Leu

<210> 825
<211> 21
<212> PRT
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<400> 825
Pro Tyr Ser Glu Ser Xaa Xaa Asn Ser Leu Ala Val Val Leu Gln Arg
1 5 10 15

Arg Asp Xaa Glu Asn
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<210> 826
<211> 56
<212> PRT
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<223> Xaa equals any of the naturally occurring L-amino acids

<400> 826
Met Ser Glu Ala Cys Ile Val Ile Ile Ser Tyr Phe Phe Pro Leu Asp
1 5 10 15

Pro Ser His Gln Met Phe Val Asp Phe Ile Arg Ile Phe Lys Leu Pro
20 25 30

Ala Ser Gly Phe Val Glu Leu Gly Ile Ser Val Ser Leu Ile Phe Xaa
35 40 45

Leu Leu Ser Cys Thr Tyr Phe Xaa
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<210> 827
<211> 54
<212> PRT
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<400> 827
Asn Ser Lys Xaa Ile Thr Ile Lys Lys Ala Gly Thr Pro Ala Gly Thr
1 5 10 15

Gly Pro Glu Phe Pro Gly Arg Pro Thr Arg Pro Thr Ala Ala Arg Arg
20 25 30

Arg Gln Lys Gly Thr Ala Ala Arg Xaa Arg Gln Lys Gly Ala Xaa Glu
35 40 45

Arg Arg Arg Gln Lys Gly
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<210> 828
<211> 78
<212> PRT
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<400> 828
Leu Val Phe Thr Glu Thr Leu Arg Glu His Lys Phe Met Gly Phe Leu
1 5 10 15

Met Met Ile Leu Leu Gly Ile Met Ser Tyr Ser Leu Ser Ser Leu Met
20 25 30

Asn Val Lys Leu His Cys Ser Gln Arg Phe Xaa Leu Leu Ser Thr Ala
35 40 45

Ile Asn His Gly His Ser Pro Xaa Asn Ile Ile Phe Phe Leu Leu Lys
50 55 60

Glu Lys Asn Gly Lys Lys Leu Gln Gly Asn Gly Asn Tyr Tyr
65 70 75

<210> 829
<211> 89
<212> PRT
<213> Homo sapiens

<400> 829
Ser Ala Glu Glu Lys Lys Leu Thr Arg Ile Pro Ser Val Thr Ala Ser
1 5 10 15

Glu Gln Gly Arg Ala Gln Arg Arg Ile Pro Ala Pro Arg Arg Gly Ala
20 25 30

Gly His Val Ala Tyr Gly Arg Pro Ala Pro Arg Arg Arg Ser Trp Gly
35 40 45

Ala Gln Val Leu Leu Ile Glu Ala Gln Pro Val Asp Gly Val Arg Pro
50 55 60

Val Ala Ala Pro Gly Ala Pro Gly Pro Gly Leu Pro Gly Val Gly Leu
65 70 75 80

Leu Gly Asn Ala Ala Gln Ser Gly Trp
85

<210> 830
<211> 43
<212> PRT
<213> Homo sapiens

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<400> 830
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Pro Leu Ile Phe Ile Asn Ser Arg Ile His Thr Asp Ser Pro Gly Ile
 1               5                  10                  15

Val Pro Ser His Ser Glu Asp Ala Leu Arg Thr Leu Gln Ile Leu Leu
            20                  25                  30

Pro Tyr Ile Thr Leu Asn Ser Gly Leu Arg Xaa
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<210> 831
<211> 110
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<213> Homo sapiens

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Lys Asp Ser Leu Asp Ser Gly Lys Leu Leu Gly Ser Gln Leu Gln Phe
 1               5                  10                  15

Ile Thr Val Lys Gly Gln Arg Leu Arg Ser Ala Lys Gly Gly Gly Ala
            20                  25                  30

Gln Xaa Arg Ser Thr Thr Asp Glu Ala Thr Ala Ser Ile Cys Pro Leu
        35                  40                  45

Pro Val Glu Pro Tyr Arg Gln His Leu Ile Leu Thr Ala Thr Cys Asp
    50                  55                  60

Asn Xaa Gln Glu Val Leu Pro Ile Leu Pro Thr Arg Ala Ala Ser Leu
65                  70                  75                  80

Gly Asp Leu Cys Val Pro Xaa Phe Xaa Val Cys Leu Gly Asp Arg Val
                85                  90                  95

Trp Xaa Xaa Leu Gly Arg Xaa Arg Val His Gly Gly Asp Ser
            100                 105                 110
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<210> 832
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<212> PRT
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<400> 832
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Gln Arg Ser Ile Leu Val Thr Trp Phe His Cys His His Leu Val Asp
 1               5                  10                  15

Val Gln Phe Xaa Thr Ile Leu Ser Ala Pro Ser Gly Ser Leu Ala His
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20 25 30

Ser Leu Leu Cys Asn Cys Trp Arg Ile Thr Ala Glu Phe Leu Ala Val
35 40 45

Leu Ser
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<210> 833
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<212> PRT
<213> Homo sapiens

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<400> 833

His Leu Lys Leu Leu Gly Leu Glu Arg Xaa Gln Arg Xaa Ser Gly Arg
1 5 10 15

Xaa Thr Thr Leu Gly Gly Arg Ser Thr Gly Leu Val Ile Glu Leu Xaa
20 25 30

Leu Xaa Arg Leu Leu Xaa Cys Xaa Met Asn Cys Asn Ile Cys Leu
35 40 45

<210> 834
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<212> PRT
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<400> 834
Glu Xaa Xaa Thr Glu Gly Tyr Gly Cys Glu Arg Arg Gln Lys Gly Thr
1 5 10 15

Ala Ala Arg Arg Xaa Gln Lys Gly Thr Ala Ala Arg Arg Arg Gln Lys
20 25 30

Gly Thr Ala Ala Arg Arg Arg Gln Lys Gly Thr Ala Ala Arg Arg Arg
35 40 45

Gln Lys Val Arg Leu Arg Glu Asp Asp Arg Arg Ile Arg Leu Arg Glu
50 55 60

Asp Asp Arg Arg Glu Asn Leu Ser Ser Thr Leu Asn Leu Pro Thr Glu
65 70 75 80

Pro Ser Lys Ser Pro Cys Lys Phe Asn Cys
85 90

<210> 835
<211> 51
<212> PRT
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<400> 835
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Asp Ile Xaa Leu Val Phe Ile Leu Lys Gln Phe Leu Gly Leu Phe Arg
  1               5                  10                  15

Gly Ser Leu Cys Cys Leu Tyr Cys Ile Asp Leu Xaa Tyr Arg Cys Leu
             20                  25                  30

Phe Ile Lys Lys Lys Ile Gln Lys Xaa Lys Lys Lys Ile Asn Lys Xaa
         35                  40                  45

Lys Lys Xaa
     50
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<210> 836
<211> 47
<212> PRT
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Ser Ser Leu Gln Lys Asn Leu Val Leu Glu Tyr Phe Leu Lys Gly Ile
1   5   10   15

Leu Asn Thr Ile Lys Thr Ala Phe Phe Phe Pro Ala Ser Ile Gln Pro
            20   25   30

Thr Trp Phe Cys Phe Asn Lys Ser Leu Glu Lys Leu Ile Xaa Xaa
        35   40   45

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<211> 733
<212> DNA
<213> Homo sapiens

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tctcccggac tcctgaggtc acatgcgtgg tggtggacgt aagccacgaa gaccctgagg 180
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catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctggtc aaaggcttct 480
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acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat gaggctctgc 660
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gactctagag gat 733

<210> 838
<211> 5
<212> PRT
<213> Homo sapiens

<220>

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Trp Ser Xaa Trp Ser
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<210> 839
<211> 86
<212> DNA
<213> Homo sapiens

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cccgaaatat ctgccatctc aattag 86

<210> 840
<211> 27
<212> DNA
<213> Homo sapiens

<400> 840
gcggcaagct tttgcaaag cctaggc 27

<210> 841
<211> 271
<212> DNA
<213> Homo sapiens

<400> 841
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gcccctaact ccgcccagtt ccgcccattc tccgccccat ggctgactaa ttttttttat 180
ttatgcagag gccgaggccg cctcggcctc tgagctattc cagaagtagt gaggaggctt 240
ttttggaggc ctaggctttt gcaaaaagct t 271

<210> 842
<211> 32
<212> DNA
<213> Homo sapiens

<400> 842
gcgctcgagg gatgacagcg atagaacccc gg 32

<210> 843
<211> 31
<212> DNA
<213> Homo sapiens

<400> 843
gcgaagcttc gcgactcccc ggatccgcct c 31

<210> 844
<211> 12
<212> DNA
<213> Homo sapiens

<400> 844
ggggactttc cc 12

<210> 845
<211> 73
<212> DNA
<213> Homo sapiens

<400> 845
gcggcctcga ggggactttc ccggggactt tccggggact ttccgggact ttccatcctg 60
ccatctcaat tag 73

<210> 846
<211> 256
<212> DNA
<213> Homo sapiens

<400> 846
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caattagtca gcaaccatag tcccgcccct aactccgccc atcccgcccc taactccgcc 120
cagttccgcc cattctccgc cccatggctg actaattttt tttatttatg cagaggccga 180
ggccgcctcg gcctctgagc tattccagaa gtagtgagga ggcttttttg gaggcctagg 240
cttttgcaaa aagctt 256

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/05881

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/04; C07K 5/04, 16/00; G01N 33/53
US CL : 536/23.1; 530/300, 387.9; 436/501
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 530/300, 387.9; 436/501

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

East, GenEmbl, EST, GeneSeq, PIR-63, SwissProt, SPTREMBL, Issued patents sequence database: SEQ ID NO:1 and monoamine adj oxidase

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	ZHU et al. Promoter organization and activity of human monoamine oxidase (MOA) A and B genes. J. Nuerosci. November 1992, Vol. 12, No. 11, pages 4437-4446, especially pages 4438-4439.	1-12, 14-16, 20-23 -------- 13, 17-19
X ----- Y	CHEN et al. The deduced amino acid sequences of human platelet and frontal cortex monoamine oxidase B are identical. J. Neurochem. July 1993, Vol. 61, No. 1, pages 187-190, especially pages 188-190.	1-7, 11-12 ---------- 19
X ----- Y	GRIMSBY et al. Human monoamine oxidase A and B genes exhibit identical exon-intron organization. Proc. Natl. Acad. Sci., USA. May 1991, Vol. 88, pages 3637-3641, especially 3638-3640.	1-12, 20-21 and 23 --------- 17-19

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
01 JUNE 2000	05 JUL 2000

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MARJORIE MORAN JOYCE BRIDGERS PARALEGAL SPECIALIST CHEMICAL MATRIX
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Form PCT/ISA/210 (second sheet) (July 1998)*

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ------ Y	BACH et al. cDNA cloning of human liver monoamine oxidase A and B: Molecular basis of differences in enzymatic properties. Proc. Natl. Acad. Sci., USA. July 1988, Vol. 85, pages 4934-4938, especially pages 4935-4936.	1-16, 20-23 ---------- 17-19
Y	US 5,783,680 A (BRUNNER et al.) 21 July 1998, columns 5-15.	13, 17-19

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/05881

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchabl claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite paymer of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report cover only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report i: restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
   1-23, SEQ ID NO:1

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-10 and 21, drawn to isolated nucleic acid sequences, a gene, a recombinant vector and host cells comprising the sequences.
Group II, claim(s) 11-12 and 14, drawn to an isolated polypeptide and a recombinant host cell expressing the polypeptide.
Group III, claim(s) 13, drawn to an antibody.
Group IV, claim(s)15-16, drawn to a method of making a polypeptide and the polypeptide made.
Group V, claim(s) 17, drawn to a method of preventing, treating, or ameliorating a medical condition by administering a polypeptide or a polynucleotide.
Group VI, claim(s) 18, drawn to a method of diagnosis using a polynucleotide.
Group VII, claim(s) 19, drawn to a method of diagnosis using a polypeptide.
Group VIII, claim(s) 20 and 23, drawn to a method of identifying a binding partner to a polypeptide.
Group IX, claim(s) 22, drawn to a method of identifying biological activity.

In addition, each isolated nucleic acid represented by SEQ ID NO: X is a separate product, not necessarily related to any other nucleic acid represented by SEQ ID NO: X. Each polypeptide is likewise considered a separate product, not necessarily related to any other polypeptide sequence, or to any nucleotide sequence. Applicant is required to elect either ten nucleic acid sequences or one polypeptide sequence for search.

The inventions listed as Groups I-IX do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: every nucleic acid sequence claimed is not unique (SEQ ID NO: 1 is not unique, see the Search report), and therefore does not represent a special technical feature. As the nucleic acid would be the "linking" feature, and the nucleic acid is not a special technical feature, the claims do not relate to a single inventive concept. Because there is no single inventive concept, a method of use is not included with the nucleic acids of Group I.

Although unity of invention is lacking for Groups I-IX, as previously set forth, no invitation to pay for a search for extra groups has been made. However, unity of invention is also lacking with regard to sequences and applicant was invited to pay for a search for additional groups of sequences. Applicant elected only SEQ ID NO:1, therefore no extra search fees are due.